W. RALL

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See p. 174

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See p

Research & Computation Diary
(continued from Book 5)

This begins in January 1965

goes thru July 2, 1965

1/5/65 (Tuesday)

New page, new book, new year, new optimism? Yesterday went to dentist, hopefully to finish siege of dental work. Past month & especially past week were undermined by toothache, combined with "battle fatigue" & holiday distractions — but toothache was a very real trigger of considerable depression of scientific morale. Today, hope to return to optimistic track & — with help of aspirin — return to resolve of 12/3/64 (page 77 of Book 5) to write in mornings and defer distractions to afternoon. However, at least today, relax rigidity to permit mornings also for strategy & abstracts etc.

Deadlines ahead, many of which should be anticipated

(a) Feb. 1 deadline for Tokyo abstract
(b) early Jan for ~~Fender's~~ Cal-Tech abstracts ✓
(c) March 5-8 Cal Tech lectures
(d) July ~~1st or 2nd~~ 3rd week — Gordon Conference
(e) late July ~~& early August~~ at Bethany Beach
(f) Sept. in Tokyo (? L.A.)

Re Tokyo abstract, I had been planning to work up the spatial inhibition degeneracy & potency story, but came to realization this morning that it would be less schizi to ~~present~~ prepare Mitral story for Tokyo, because then would not conflict with task of finishing paper; i.e. it is both efficient, practical & morale boosting to combine the two tasks into one.

Some Problems in Developing a Theory of Dendritic Neurons

1/5/65

Among other things, figures for mitral paper & slides for Tokyo become a common objective. Also, it seems very likely that mitral study would be of more interest to regular neurophysiologists. The inhibitory story is probably more for modelers and biophysicists. Also, I will feel less conflicted about working out numerous details, as they relate to the mitral story: ~~Even~~ also the related project with Phil Nelson & Van Buren. After Tokyo, take up J story!

* In the next day or two, prepare abstract for Tokyo.

Today, better switch to preparing titles and abstracts for Fender

(I) Theoretical significance of dendritic trees for neuronal input-output ~~papers~~ relations. (same as Ojai)

(II) ? ~~Paradoxes in matching experiments and theory~~
Problems and paradoxes ~~in~~ the quantitative study ~~parameters~~ characterizing of dendritic branching.

(I) would emphasize non-linearity & spatiotemporal pattern as in Ojai paper & relevance to nerve nets.

(II) would touch more on anatomy, τ, λ, L/λ, ρ, safety factor (? Aitken & Bridger) - problem in introduction

1/5/65

for Tokyo Abstract, title could be same as ditto, or

Theoretical Reconstruction of Potentials Recorded in the Rabbit Olfactory Bulb in Response to Synchronous Antidromic Activation.

~~Theoret~~ shorter title could be

Theory for Computation of Olfactory Bulb Antidromic Potentials

Points to cover: Periods I & II – Mitral; Period III granule

Punctured Symmetry & Potential Divider Effect

Neg peak not a propagation velocity.

Active vs Passive Dendrites

Synch. Dendritic Spike vs electrotonic attenuation.

Question of L/λ & hot & cool.

May need to reread notebooks

1/7/65 Wrote Gordon yesterday, writing ~~Fender~~ with abstract today & hope to deal with Tokyo abstract ~~tomorrow~~. Toothache is still with me. Woke me last night. Aspirin cuts the pain, but not sure it restores drive. This morning spent time discussing with Jose & John Stephenson re John's publication situation. Also, yesterday, learned that Gordon Conference is to be July 19–23 at Andover, N.H. Proctor Academy

note: That last year's announcements appeared in the March 13, 1964 issue of Science

Also, yesterday collected information on group flights to Tokyo.

1/8/65 Got off letter, started on abstract for Tokyo; completed a first draft which was sent to Gordon

J K L M N O P Q R S T U V W X Y Z

1/15/65

In Tokyo Abstract, title would be same as the ..., or
"Theoretical Reconstruction of Potentials Recorded in the Rabbit Olfactory Bulb in Response to Synchronous Antidromic Activation."
Shorter title could be:
"Theory for Computation of Olfactory Bulb Antidromic Potentials"

Points to cover: Periods I + II — Mitral; Period III — Granule
Positivity — Symmetry & Potential Divider Effect
J Why peaks not a propagation velocity
K Active vs Passive Dendrites
L Synaptic Dendro-dendritic [illegible] to [illegible] electrotonic
Question of t/λ + [illegible].
May need to revised [illegible]

1/17/65 Wrote Gordon yesterday, writing [illegible] today a letter to deal with Tokyo abstract tomorrow. Toothache is still with me. Woke me last night. Aspirin cuts the pain, but not sure it resolves trouble. This morning spent time discussing with Jane + John Stephenson re John's publication situation. Also, yesterday, learned that Gordon Conference is to be July 19–23 at Andover, N.H. Notes that last year's announcements appeared in the March 13, 1964 issue of Science [illegible]. Also, yesterday, collected information on group flights to Tokyo.

1/18/65 Got off letter, started on abstract for Tokyo; completed a first draft which was sent to Gordon.

1/12/65

Reading José's copy of "Adaptive Control Processes"
a Guided Tour
By Richard Bellman.
Princeton 1961
(based on a set of invited lectures)

Introduction useful + shows how much he restricts problems.

p.13

* Interesting to me that on 1st page of Chapt. 1, he emphasizes some points that I have often emphasized "... concepts play a role equally important with that of equations, and the construction and interpretation of mathematical models is of even greater significance than the solution of the particular equations to which they give rise." earlier on the same page, he wishes "to lay bare the many approximations that are consciously or unconsciously made in studies of this type" and later "Only if we are very clearly — almost painfully — aware of the manifold aspects of the problems that arise, can we hope to select pertinent mathematical models and utilize meaningful mathematical techniques."

p15 wants simplifying assumptions to be explicit. also "What is remarkable is that deep understanding of many physical processes can be obtained from rudimentary assumptions."

1/13/65

"Optimization Theory and the Design of Feedback Control Systems" Charles W. Merriam III (General Electric)
McGraw-Hill 1964

Interesting new text with most recent post-war perspective

Preface makes acknowledgement to Bellman & also to Pontryagin.

Introduction traces evolution of control theory stimulated by World War II

i.e. Automatic Control Theory went from cascaded systems to feedback systems.

* sensitivity, stability & performance formulated mathematically.

Transform methods involving complex variable theory frequency domain analysis.

New pressures created by need for systems to operate in outer space.

"Currently, the applied mathematician is succeeding in formulating feedback control theory on a profound mathematical and conceptual basis.* The stability theory of Lyapunov, the topics of observability and controllability originated by Kalman, and the mathematical optimization theories of Bellman and Pontryagin are notable contributions to the mathematical theory of automatic control."

* Philosophically, optimization theory is an attempt to provide a means for <u>direct system synthesis</u> as opposed to system synthesis via repeated analyses of controllers selected on a trial-and-error basis. From practical standpoint, ~~system~~ have advantage of spec & solve in time domain. Avoid many problems of freq. domain; furthermore, frequency domain methods essentially are limited to linear time-invariant systems.

Q R S T U V W X Y Z

In this connection note pp. 12-13 of Merriam ←

He distinguishes between

parameter optimization

impulse response optimization

system optimization

but all cases, result from minimizing some error index

system optimization is supposed to select both the configuration & component values, but presumably the number and kinds of components must be pre-specified.

Wonder how truly opt. configuration is found.

Question also about adequacy of error measure.

For analog computations, a good example of state signals is the output signal of the integrators used to solve a system of diff. equations.

1/13/65

Jose & ~~I~~ agreed in conversation that it would be well to survey Mesarovics ~~book~~ to decide if base a study seminar on it & also to ponder ← the wider question of applicability of optimization theory to current problems of biology.

p.5 Merriam claims that the concepts of <u>response extrapolation</u> (which is the basis for system stability), and <u>desired response prediction</u> (which is the basis for system performance) are the crux of all control problems.

p.7 $m_1(t), m_2(t), \ldots, m_M(t)$ are control signals, or inputs, or independent variables <u>of the dynamic process</u>

$q_1(t), q_2(t), \ldots, q_Q(t)$ are response signals, or outputs, or dependent variables <u>of the dynamic process</u>

↑ these need not be physical variables, but

$x_1(t), x_2(t), \ldots x_N(t)$ are state signals (outputs)

state signals are not ~~generally~~ generally associated with frequency domain techniques.

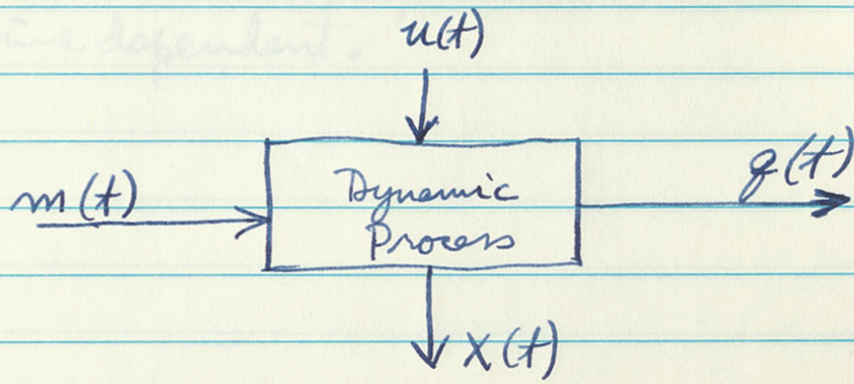
Exclude hysteresis (memory) & similar phenomena

∴ dynamic process is <u>state-determined</u>. i.e. if state is completely defined at one particular time, it is determined for all times. (For some peoples, this seems to be the definition of a <u>dynamic process</u>). My thought is that ~~———~~ hysteresis can be interp. as apparent phenom. due to incomplete set of state variables.

1/13/65 add a fourth set of variables (second set of inputs) called "load disturbance signals"

$$u_1(t);\ u_2(t),\ \ldots\ u_N(t)$$

Diagram of dynamic process



regard $\vec{m}(t)$, $\vec{q}(t)$, $\vec{u}(t)$ and $\vec{X}(t)$ as column vectors having M, Q, N, N components

Using vector notation, ~~without arrows~~

D.E. $$\dot{\vec{X}}(t) = \vec{f}\left[\vec{X}(t), \vec{m}(t), t\right]$$

where $\vec{f}$ has a dependence upon time caused by load disturbance & possibly also because of time varying coeffs.

this is state equation, sometimes use particular case

$$\dot{\vec{X}}(t) = B\vec{X}(t) + C\vec{m}(t) + \vec{u}(t)$$ W

where B and C are matrices X

general response equation is $\vec{q}(t) = \vec{g}\left(\vec{X}(t), t\right)$ Y

Z

& spec. case is $\vec{q}(t) = A\vec{X}(t)$

where A is a matrix

1/13/65

p. 9 note that "saturation equations" may be needed.

If the process is linear, saturation does not occur.

The matrices A, B, C have elements which, in general, are time dependent.

~~If~~ If $\beta = 0.1$, then G_r can be interpreted as consisting of $\varepsilon = 0.09$.

Want $\left.\begin{array}{l} \varepsilon + J = 1 \\ \varepsilon = 0.1 J \end{array}\right\}$ $\therefore$ $J = 0.91$

$\varepsilon + J = 1.0$

1/14/65

Time to settle down to writing again next week. Yesterday reading in Control Theory books. Also Hodgkin gave N.I.H lecture: Movies of squid + cuttlefish + of rolling axoplasm out of squid fiber. Reversing inside + outside electrolyte reverses resting potential but do not get action potential, because of a permeability asymmetry (not specified). ~~Cole~~ Also pointed to some results of Fütgan, at Cambridge, showing that as muscle contraction is blocked by cyanide, muscle impulse becomes more nerve like. Prawns have myelinated fibers. Cole's concluding remarks placed emphasis upon key importance of Hodgkin's concern (throughout the war) with the action potential overshoot. He implied that this had been the key to subsequent success in terms of the Na, K conductance story. I would guess that he has decided that this was the key point that he himself had failed to make the most of. Hodgkin did refer to learning the squid prep. from Cole and also later, that Cole invented voltage clamp.

Apparently Chandler & Meves have worked with Hodgkin to calc. zeta potential for fixed charge inside axon membrane which accounts for discrepancies between low & high ionic concentrations inside. Get a figure for the distance between fixed charges.

Thoughts last night. Must get out short note on action pot. model and to take care of anodal break excitation, may need to permit neg G_j up to the amount that is implicit in $G_Σ$ (ie may need footnote to express $G_Σ$ as a linear comb. of $G_ε$ + G_j), this permitting G_j neg up to this amount. Also even function of $G_ε$ vs V would help anodal block excitation & is probably O.K. May want to check. Also might conceivably mimic Kandel's anomalous rectification.

1/14/65

See Ted Lewis tomorrow afternoon

Check list for now & next week.

(1) revise Tokyo abstract & complete registration

(2) resume Mitral manuscript & figures

(3) as soon as possible on action pot. model (see previous page)

(4) seriously consider short note on potential divider story, because of relevance to other situations. Need to check to see what Bill Hagins has done & what he knows of others.

On the Tokyo abstract can save space by not specifying the depths, since they are not used. Perhaps improve other sentences. Also, could refer to latency with distance giving only an apparent conduction velocity?

Also, think about how potential divider effect gives results which differ from single unit in volume conductor. Do this by means of equations.

This assumes that a few cylindrical shells from axon gets one to effectively zero potential

work from $V_i(x)$

compare $V_e \propto I_m \propto \frac{\partial^2 V_i}{\partial x^2}$ Lorente & Plonsey

which is simply not true in palisade.

with $V_e = V_{e_0} + \int \frac{r_e}{r_i} \frac{\partial V_i}{\partial x}$

of this form

In particular; entirely different when $\frac{\partial V_i}{\partial x} = \text{const.}$

Also, different in general consider 

May want concise theoretical paper which says it will be numerically illustrated elsewhere.

1/15/65

Ted Lewis claims that he can fit all of the locus type behavior seen in cardiac ganglion by means of adjusting params of his analog to H&H functions. He does not use m, n & h, he simulates the dependence of g_K & g_{Na} upon V and time.

Had lunch & visit with Ted & Librascope associate and Bob Taylor & Dick FitzHugh. Discussed many things. Taylor reported some of the recent results from the Miami meeting he had just attended. Lewis was particularly concerned about his assumption which replaced absolute $V_m - V_0$ with ΔV as the variable det g_{Na}

* Lewis specifically asked me to provide him with examples of where theory predicted expt. in the course of my research. Harmon had mentioned this to him & he was not sure of specifics. I answered re monosynaptic input output & gave him those reprints, but actually, I have a number of examples that are at least somewhat relevant.

① The 1957 paper "predicted" $\tau \sim 4$ msec and delayed transmitter → 0. Also 1960 paper presented theory ~~for~~ Nyquist plot. These predictions confirmed by my 59 paper & in fact by Eccles 61 paper.

② 53 + 57 abstract predicted rapid soma equilization time const.

③ 1955 input-output theory called for segments of sigmoid & expt, when properly interp. - confirmed this. Of course "random" method - Also, the single parameter.

④ Rall & Hunt — again predicted & confirmed sigmoid shift.

1/18/65 further examples

(5) Extracellular pot theory - decrement with distance
also pos. pot. following neg.

(6) Soma equalization rapid time constant

(7) also, notion of J at soma 1960 IPSP time course
1961-62 potency.

In writing to Ted point out matters of degree
i.e. (A) prediction followed by expt.
(B) " " " reinterp. of expt.
(C) expt. interp problem ⟶ theory

Re kinetic model, must take a second look at papers that Mueller wrote from Rock. Inst. to see if they have anything in common with my model.
(1/22/65) seems not to.

Re gradients in cortical layer, must recheck Tasaki and Lorente. The more I think about it, the more I suspect that most people have just not thought out these gradients, as to what they really represent. There is vague talk of dipoles, but the gradient in field of single dipole is very different from that of layer. May need to refer to Helmholtz - Woodbury - Gloor treatment for region outside, but not inside layer. The need, unfortunately, is for a careful presentation of the ideas and implications.

1/18/65

? short papers to Science or other journals re material to be revealed Cal. Tech.; Gordon; Tokyo.

(1) Syndromous symmetry story
(2) action potential kinetics story
(3) antidromic invasion story
(4) factors in the potency of synaptic inhibition
(5) math. for small group of dendritic neurons

? for Gordon Conference — not sufficient to let several point units represent a neuron, because of several differences

(A) neighboring compartments of same neuron influence each other $g_{ij} = g_{ji}$ (a) bidirectionally, (b) graded, (c) continuously

(B) axon to neuron assumed to be (a) unidirectional, (b) all-or-nothing (c) brief.

∴, If incorporate both into a single matrix
electrotonus has $g_{ij} = g_{ji}$
whereas synaptic has $g_{ij} = \delta(t)$ and $g_{ji} = 0$

Conceivably, for a repet. neuron, could have string of $\delta(t)$, but this not really necessary if let repet. be generated within the model.

However, still think will need separate set of matrices for effects of activity in other neurons upon E + I of each compartment.

213- 478-9711 - Ext 2081 UCLA

1/18/65 Larry Stark phoned me 1/15/65 re Gordon Conference Program which is now being finalized relative to what he told me last Fall

Session Chairman

Otto Schmidt EKG

Mason - Sensory Commun. - McCann & Langer (~Hartline)

Stark - Math CNS - McCulloch & Suto (MIT - Lettvin frog retina)

Taxonomic Pattern - Takahashi & Juliano (Arthur D. Little)

Bartholomay - Stochastic - Stephenson & Barucha Reed

Barnet - Non-Linear Control Systems - Bellman - Otto Smith (Berkeley)

Landahl - Rashevsky - Hist. Math Biol.

- Training Session - Use of Computers in Training - Perliss, Talbot & other

Rall - Math. Biophys - { Attinger - Pressure Flow relations in circulation
? 1/19/65 Dick FitzHugh
Math Models of Excitation & Propagation

July 19-23 at Andover, N.H.

1/22/65 Further revision of Tokyo Abstract.
Send off Tokyo Registration forms & check.
It does seem that the toothache siege is finally over.

1/27/65 Superposition Time Scale

Looking at mitral, axon, granule, superposition

figure That was based upon short passive with flat F.C.

64795.9041

Time scale of original plot of 8 computed series was 20 KT to the inch.

~~Af~~ τ = 4 to 5 msec

~~Now~~ DT = .01, ∴ 1" equals 0.2τ ≈ 0.8 to 1 msec
½" equals 0.1τ ≈ 0.4 to 0.5 msec

And The ticks of the final figure are at 1" intervals

~~Also, note that GL~~
But note that final figure was translated slightly; almost exactly 0.1" so that origin of final figures corresp to KT = 1 (T = 0)
first tick corresp to KT = 21 T = 20(DT)

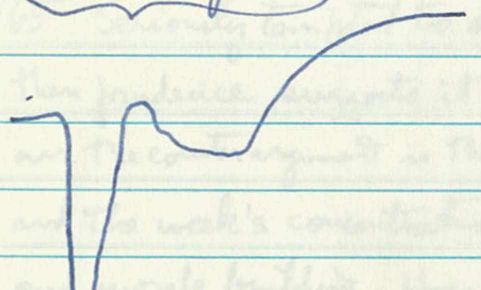
GL was cpt. 9
PL was cpt. 7
MBL was cpt. 4
GRL was cpt. 2
} of 64795.9041

Now, for active dendrites use 64795.9059 mitral to superimpose with granule only.

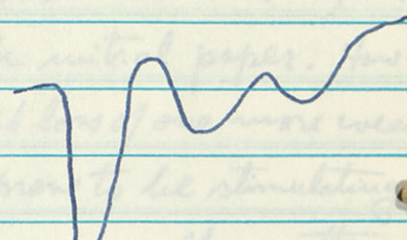
GL ~~was~~ cpt. 14
PL cpt 11
MBL cpt. 4
GRL cpt. 2
} tried for two difference granule latencies.

4/27/65 Now try to assess this + earlier superposition against the exp series provided by Gordon.

One important point is that Active dendrite case does not fit very well at MBL and GRL although it fits OK at GL & PL. The period II positivity appears too large and too sharp in the superpos. as compared with the data. At MBL, the data show the period II pos. to be sig. smaller than than the neg. (in abs. value), notice that March 30 prod 2 shows periods II & III well separated



also April 12, prod 3



Now, the problem here is that a pretty strongly diphasic granule is needed to produce this. More than seems reasonable.

Also, at GRL, granule pos. would have to be very sharp + large & perfectly timed to prevent a substantial dip that is not seen experimentally.

This begins to look like an argument in favor of the passive case, with the slow fall of a smaller mitral (+) requiring less perfect timing of granule pos.

3rd try shows this can be done, but is this too specific? Still problem at MBL

1/28/65

Paradox. I feel I should write up action pot. kinetics and punctured symmetry, although I don't have figures ready & also, with mitral paper, remaining figures are an obstacle, yet, ~~[illegible]~~ work with Ezra & with spherically sym. neuron has figures already prepared from 1961 Congress & this is still not written up. Would make more sense to finish up the old work for which figures are ready, or nearly ready. However, could write brief notes for Science on the two items first mentioned. My 1957 Science paper was worthwhile.

1/29/65 Seriously tempted to devote one solid week to a paper on these kinetics, but then prudence suggests it would be wiser to finish mitral paper. However the counter argument is that mitral paper can surely stand loss of one more week and the week's concentration on the other task could prove to be stimulating and morale building. Hope to build up steam this way, as well as getting the note done. Maybe this could become a pattern: occasionally, when things are lagging, take out a week for concentrated effort on a short note; this would be similar to having to take time out to prepare lectures or seminars, & could even lead to that as well.

1/29/65 Lunch conversation with Bill Hagins brought out the point of view (Cambridge & U.C. Lond.) that a good theoretical biophysicist ought to be able to design the best experiments & furthermore, the implication that this is the best thing for him to do. i.e. most likely to be important & recognized as such. He thought that synaptic transfer fcn from presynaptic potential to postsynaptic pot. is a crucial unsolved problem (of course, I have done part of it, but how complete). Also good expt design for dendritic λ and τ needed.

$$\frac{d\varepsilon}{dt} = k_1 V^2 + k_2 V^4 - (k_3 + k_4 j)\varepsilon$$

$$\frac{dj}{dt} = (k_5 + k_6 j)\varepsilon - k_7 j$$

for $\dot{j} = 0$ $\quad \varepsilon_{ss} = \frac{k_7 j}{k_5 + k_6 j}$

for j small, $\varepsilon_{ss} \rightarrow \frac{k_7}{k_5}$

2/1/65

For isolated membrane, consider

$$\frac{dV}{dT} = -V + (1-V)x - \left(\frac{V-\beta}{\cancel{\beta+V}}\right)y + \psi$$

$$\frac{dx}{dT} = a_2V^2 + a_4V^4 - (b_1 + b_2 y)x$$

$$\frac{dy}{dT} = (c_1 + c_2 y)x - c_3 y$$

see opposite page

New notation not adopted here but yes

see next page

where $\frac{c_1}{c_2} \overset{\text{need}}{\underset{\text{not}}{\cancel{=}}} \frac{b_1}{b_2}$ as in earlier versions

note $y, \varepsilon, g \rightarrow V, x, y$

Now look back to Book 4, pp. 35–55

Compared with p. 38, here $\dot{y}=0$ gives $y_{ss} = \frac{(c_1 + c_2 y)x}{c_3}$

$\varepsilon_{ss} = \frac{c_3 g}{c_1 + c_2 g}$

and $\dot{x}=0$ gives $x_{ss} = \frac{a_2V^2 + a_4V^4}{b_1 + b_2 y}$

cf. pp 47 & 48 of Book 4 also $\dot{V}=0$ gives $V_{ss} = \frac{x_{ss} + \beta y_{ss} + \psi}{1+x+y}$

Problem is to decrease ~~x~~ below y for small V and y

Previous $R_3 \gg R_4$ by factor 10 to 50

That means here, initially $c_1 \gg c_2$ and $b_1 \gg b_2$

Hence, for y_{ss} small, $x_{ss} \approx \frac{c_3}{c_1} y_{ss}$

∴ increasing c_1 without necessarily increasing b_1 would probably help. This would permit y to build up without (perhaps) pulling x down quite so hard.

See p. 33

2/2/65 5/28/64 2/2/65

Modify WXR ~~751~~C → 752C

so that $\frac{dJ}{dT} = (R_5 + R_6 J)E - R_7 J$

This means new numbering

Change a statements 300 + 310 + drop 320, 330 + 340 which used old R(7) as $R_7 * V * J$

300 was QGRO = R(5) * ELOSS

now becomes QGRO = (R(5) + R(6) * Y) * X

310 was QLOSS = R(6) * Y

now becomes QLOSS = R(7) * Y

Setup a run similar to old series 5 + 6 + 7

	old $R_5 \times R_3$ = new R_5	$R_5 * R_4$ = new R_6
#5	.05 × 50 = 2.5	.05 * 1 = .05
#6	.1 × 50 = 5.	.05 * 1 = .05
#7	.05 × 50 = 2.5	.05 * 2. = .1

want R_3 smaller, but R_5

Try ~~R_3~~ =

		R_3	R_4	R_5	R_6	R_7	R_4/R_5	R_7/R_6
	6501	25	2	5.	.1	10.	2	100
rel #7		half	same	double	same	~~10.~~ same		
						10.		
Try also	6502	25	2	1.	.1	10.	for more delay	

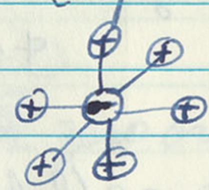
2/3/65 Phone call from Phil Nelson reminded me of the problem & suggested to him & Van Buren in comparing pos & neg of unit & population fields of motoneurons.

Phil's more careful review of the data seems confirmatory. Van Buren can see 3 or 4 unit contributions to neg, but essentially smooth graded pos. ∴ Rough hunch is that only nearest neighbors add for neg. whereas ~~two~~ or three or more shells of neighbors add for pos.

~~Two~~ Two approaches: (1) use experimental decrements with dist.
(2) consider ~~the~~ theoretical differences.

Theoretical

Compare addition of dipoles (in parallel) 

With superimposed quadrupoles 

~~For~~ dipole field, potential $\propto \frac{1}{r^2}$ $(n=1)$

quadrupole, $\propto \frac{1}{r^3}$ $(n=2)$

order of multipole

∴ Ran into problem of how to characterize the order of a multipole.

first order multipole is a dipole where $\ominus \overset{l}{\text{———}} \oplus$ $ql = p$

the inverse square law is a consequence of $l/r = \epsilon \to 0$

suppose $+q$ at l_1 get $\frac{P_0}{r} + \frac{P_1}{r}\left(\frac{l_1}{r}\right) + \frac{P_2}{r}\left(\frac{l_1}{r}\right)^2 + \cdots$

$-q$ at l_2 get $-\frac{P_0}{r} - \frac{P_1}{r}\left(\frac{l_2}{r}\right) - \frac{P_2}{r}\left(\frac{l_2}{r}\right)^2 + \cdots$

combine to get $\frac{P_1}{r}\left(\frac{l_1 - l_2}{r}\right) + \frac{P_2}{r}\left(\frac{l_1^2 - l_2^2}{r^2}\right) + \cdots$

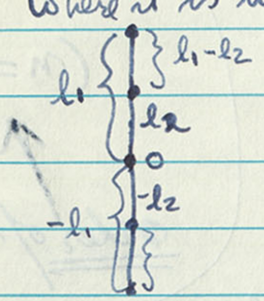
factor out $l_1 - l_2$ $(l_1 - l_2)\left\{\frac{P_1}{r^2} + \frac{P_2}{r^2}\left(\frac{l_1 + l_2}{r}\right) + \frac{P_3}{r^2}\left(\frac{l_1^3 - l_2^3}{(l_1 - l_2) r^2}\right) + \cdots\right.$

Then for $+q$ at $-l_1$ get same expressions for $P(\pi - \theta)$
$-q$ at $-l_2$ & note $P_1, P_3 \cdots$ are odd
$P_2 \cdots$ are even

Thus get $\frac{2q(l_1 - l_2)(l_1 + l_2)}{4\pi\epsilon}\left\{\frac{P_2}{r^3} + \frac{P_4}{r^3}\left(\frac{l_1^4 - l_2^4}{(l_1^2 - l_2^2) r^2}\right) + \cdots\right.$

where it is interesting that $\underbrace{(l_1 - l_2)(l_1 + l_2)}_{} = l_1^2 - l_2^2$

corresp to $l_0 l_1$ of Stratton p. 177



and that this reduces to l_1^2 when $l_2 = 0$

This also tells us that Stratton's $2l_1$ is distance between outer charges.

i.e. at right page, l is for dipole & $2l$ is quadrupole spread.

2/3/65

The other way to say this is that for pt charge at $z=+l$, we have ~~and for $r \geq l$ we have~~

$$\varphi(r,\theta) = \frac{q}{4\pi\epsilon}\frac{1}{\sqrt{r^2+l^2-2rl\cos\theta}}$$

and for $r > l$

$$\varphi(r,\theta) = \frac{q}{4\pi\epsilon}\left\{\frac{1}{r}\sum_{n=0}^{\infty} P_n(\cos\theta)\left(\frac{l}{r}\right)^n\right\}$$

$$= \frac{q}{4\pi\epsilon}\left\{\frac{P_0}{r} + \frac{P_1}{r}\left(\frac{l}{r}\right) + \frac{P_2}{r}\left(\frac{l}{r}\right)^2 + \cdots\right\}$$

for $r >> l$, get effectively only $\frac{P_0}{r}$

which can be regarded as corresponding to a zero order multipole.

1st order,

place $(-q)$ at $r=0$ i.e. have a dipole

This cancels ~~first~~ zero order term

$$\varphi(r,\theta) = \frac{ql}{4\pi\epsilon}\left\{\frac{P_1}{r^2} + \frac{P_2}{r^2}\left(\frac{l}{r}\right) + \frac{P_3}{r^3}\left(\frac{l}{r}\right)^2 + \cdots\right\}$$

To get an axial quadrupole, place $+q$ at $z=-l$ and another $-q$ at 'origin'.

This second dipole has $\varphi(r,\theta) = \frac{ql}{4\pi\epsilon}\left\{\frac{P_1(\pi-\theta)}{r^2} + \frac{P_2}{r^2}\left(\frac{l}{r}\right) + \cdots\right.$

and we note that P_1 is odd, i.e. $\cos\theta = -\cos(\pi-\theta)$ & will cancel

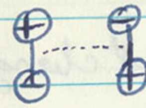
P_2 is even etc.

P_3 is odd

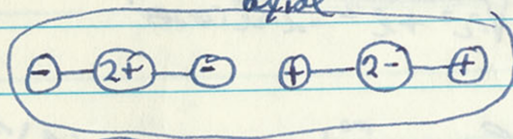
2nd order

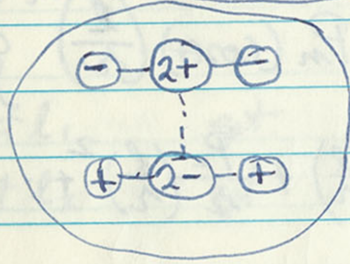
$$\therefore \text{ for quadrupole } \varphi(r,\theta) = \frac{2ql^2}{4\pi\epsilon}\left\{\frac{P_2}{r^3} + \frac{P_4}{r^3}\left(\frac{l}{r}\right)^2 + \cdots\right.$$

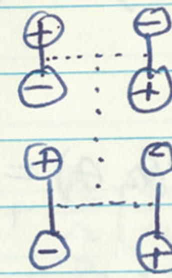
see left for displaced more fully from center

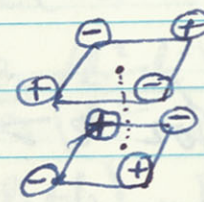
other quadrupole is 

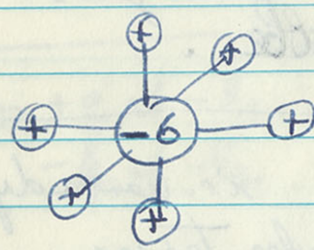
axial

Octopoles 

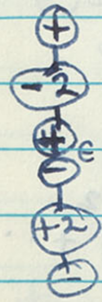
 all in plane

 all in plane

pair of planes 

But  is not higher order than quadrupoles because there is no cancellation of second order terms, there is no third limiting process, only three second order limiting processes whose effects will superpose.

but see pp 41 and 45

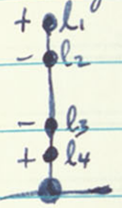


extreme

2/3/65 What would be a (third order) octopole?

Not just any superposition of quadrupole, just as quadrupole cannot be just any superposition of dipoles,

To get axial octopole, first displace quadrupole away from origin



$$\frac{P_0}{r} + \frac{P_1}{r}\left(\frac{l_1}{r}\right) + \frac{P_2}{r}\left(\frac{l_1}{r}\right)^2 + \frac{P_3}{r}\left(\frac{l_1}{r}\right)^3 + \cdots$$

$$-\frac{P_0}{r} - \frac{P_1}{r}\left(\frac{l_2}{r}\right) - \frac{P_2}{r}\left(\frac{l_2}{r}\right)^2 - \frac{P_3}{r}\left(\frac{l_2}{r}\right)^3 + \cdots$$

$$-\frac{P_0}{r} - \frac{P_1}{r}\left(\frac{l_3}{r}\right) - \frac{P_2}{r}\left(\frac{l_3}{r}\right)^2 - \frac{P_3}{r}\left(\frac{l_3}{r}\right)^3 + \cdots$$

$$+\frac{P_0}{r} + \frac{P_1}{r}\left(\frac{l_4}{r}\right) + \frac{P_2}{r}\left(\frac{l_4}{r}\right)^2 + \frac{P_3}{r}\left(\frac{l_4}{r}\right)^3 + \cdots$$

add

$$0 + \frac{P_1}{r}\underbrace{\left(\frac{l_1 - l_2}{r} - \frac{l_3 - l_4}{r}\right)}_{= 0} + \frac{P_2}{r}\left(\frac{l_1^2 - l_2^2 - l_3^2 + l_4^2}{r^2}\right)$$

$$+ \frac{P_3}{r}\left(\frac{l_1^3 - l_2^3 - l_3^3 + l_4^3}{r^3}\right)$$

$$= \frac{P_2(\theta)}{r}\left\{\frac{l_1^2 + l_4^2 - (l_2^2 + l_3^2)}{r^2}\right\} + \frac{P_3(\theta)}{r}\left\{\frac{l_1^3 + l_4^3 - (l_2^3 + l_3^3)}{r^3}\right\}$$

Whereas for $(-, +, +, -)$ below the line, would get

$$-\frac{P_2(\pi - \theta)}{r}\left(\frac{l_1^2 + l_4^2 - (l_2^2 + l_3^2)}{r^2}\right) - \frac{P_3(\pi - \theta)}{r}\left(\frac{l_1^3 + l_4^3 - (l_2^3 + l_3^3)}{r^3}\right)$$

And because P_2 is even $P_2 - P_2 = 0$

but P_3 is odd, giving

$$\frac{2P_3(\theta)}{r}\left\{\frac{l_1^3 + l_4^3 - (l_2^3 + l_3^3)}{r^3}\right\}$$

Suppose $l_4 = 0$

$l_2 = l_3 = l$

$l_1 = 2l$

Then $l_1^3 + l_4^3 = 8l^3 - (l^3 + l^3) = 6l^3$

then get $\left(\frac{12 q l^3}{4\pi\epsilon}\right)\left\{\frac{P_3(\theta)}{r^4} + \frac{P_5(\theta)}{r^4}\left(\frac{l^2}{r^2}\right)\right.$

bigger problem is that not sure r/l is big enough to make this effect important.
Closed field concept may be simpler way of presenting, although $1/r^3$ still applies to quadrupole aspect.

dipole story perhaps to consider layers.
Maybe best just to consider + compute for a finite number of cells.

also note

predict that forward axonal side of nucleus one gets no appreciable leading positivity

2/3/65

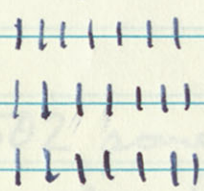
<See comment<

For motoneuron neg peak, ~~suppose~~ for nearest neuron, we have to consider radial type field like curve F of Fig. 10 of Biophys. J. paper, but for more distant ones, i.e. nearest neighbors, we may already be getting into the $\frac{1}{r^3}$ domain whereas the numbers of neighbors per shell of ~~nearest~~ neighbors should go up as r^2 (spherical surface area) to limits of nucleus.

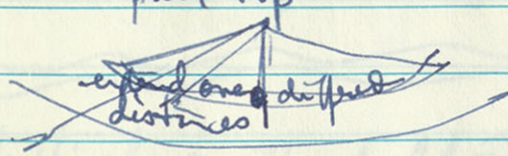
Thus, we might have 4 neighbors at r,
and 4 more at $1.414r$.
But their contribution would be $\left(\frac{1}{1.414}\right)^3 = \left(\frac{1}{2}\right)^{3/2}$
$= \frac{1}{2.82} = 0.35_3$

pos. peak

For dipole population, not sure how big l is & how coplanar the dipoles r. l is limited by fact that the current flow is very small until impulse gets close to hillock. Maybe for last node (? M spike?)



from top



Consider $\frac{\cos\theta}{r^2}$

where distance effect is $\frac{1}{r^2}$ ~~per~~ cell
but number of cells increases $\propto r^2$

∴ finite number of cells comes in plus the $\cos\theta$ factor
esp. for depth.

∴ Integrate for $\cos\theta$, where get more cells for angled cosine. Begins to lead to the Helmholtz shell story.

	peak E	peak J
6501	300.	70.
6502	567.	64.
5	415	63
6	295	82
7	345	54

2/4/65

Successful first CRT with WXR 752C

NSET	R_1	R_2	R_3	R_4	R_5	R_6	R_7
6501	500.	40,000	25.	2.	5.	.1	10.
6502	500.	40,000	25.	2.	1.	.1	10.

whereas for

WXR 751C					R_5R_3	R_5R_4	R_6
5	"	"	50.	1.	2.5	.05	10.
6	"	"	50.	1.	5.	.1	10.
7	"	"	50.	2.	2.5	.1	10.

New 6501 resembles old 6 with spike falling too fast

The fact that R_3 is halved makes the spike rise faster & peak earlier

& " " " R_4 " doubled makes J peak smaller because it makes the quenching of E by J more effective.

New 6502 somewhat resembles 7 & 5 with peak higher

Here also, R_3 halved makes spike rise faster & peak earlier

While R_5 reduced (factor 2.5) tends to delay J & permit higher E

Intuitively: Threshold $\propto R_1/R_3$ because R_3 is self loss of E

Rise of Spike $\propto R_2/R_3$

Also

If R_4 is made very small, E tends to decay passively according to R_3 it should last longer & be only weakly quenched by J & Thus also permit J to grow large without pulling down E.

If R_5 is made small, this should delay onset of J, while nonzero R6 still permits some autocatalytic growth.

2/4/65

$$\frac{dV}{dT} = -V + (1-V)\mathcal{E} - (V-\beta)\mathcal{J} + \psi$$

$$\frac{d\mathcal{E}}{dT} = k_1V^2 + k_2V^4 - (k_3 + k_4\mathcal{J})\mathcal{E}$$

$$\frac{d\mathcal{J}}{dT} = (k_5 + k_6\mathcal{J})\mathcal{E} - k_7\mathcal{J}$$

For small V where $k_2V^4 << k_1V^2$ and when $\mathcal{J} = 0$

then

$$\boxed{\begin{cases} \dfrac{d\mathcal{E}}{dT} = k_1V^2 - k_3\mathcal{E} \\[2ex] \dfrac{dV}{dT} = -V + (1-V)\mathcal{E} + \psi \end{cases}}$$

Where it can be seen that excitability increases with k_1/k_3

Note that $\frac{dV}{dT} = 0$ at peak of spike and at final st-st.

$\frac{d\mathcal{E}}{dT} = 0$ at peak of $\mathcal{E}$ and at final st-st.

$\frac{d\mathcal{J}}{dT} = 0$ at peak of $\mathcal{J}$ and at final st-st.

$$\mathcal{E} = \frac{k_7\mathcal{J}}{k_5 + k_6\mathcal{J}}$$

$$\mathcal{E} = \frac{k_1V^2 + k_2V^4}{k_3 + k_4\mathcal{J}}$$

$$V_{ss} = \frac{\mathcal{E} + \beta\mathcal{J} + \psi}{1 + \mathcal{E} + \mathcal{J}}$$

6501

also try one with $V = -.5$ KHVSD=0, KLAMP=+1

and try ~~C=0 [illegible] V=-.1 E=~~

	C	V	E	Q	KHVSD	KLAMP
	.0	-.1	.28	.12	0	-1
6502	0	-.1	.28	.03	0	-1

2/4/65 Design next runs with WXR752C

NSET	R_1	R_2	R_3	R_4	R_5	R_6	R_7
6501	500.	40,000	25.	2.	5.	.1	10.
6502	"	"	"	"	1.	"	"
				0.2			
6503	"	"	"	0.01	5.	"	10.
6504	"	"	"	0.01	1.	"	"
6505	"	"	"	0.1	0.1	"	"
6506	"	"	"	"	"	.01	"
6507	"	"	"	.01	"	"	"
6508	"	"	"	"	.01	"	"
6509	"	"	"	"	"	.001	"

Do each of these for V = .2 KHVSD = 0 KLAMP = 0

and V = .5 either +1

~~V = .7 either +1~~

C = 1. 0 " −1

7 × 3 = 21

2 × 2 = 4

25 × 10 = 250 secs est.

For voltage clamp at V=0.5

	peak C	KT	late C @ KT=90	
6501	~~-15~~ ~~-30~~	~~11~~ ~~12~~	~~+18~~ -5.6	} for V=0.4
6502	+21	20	-16.6	
6503	-30	12	+18	
6504	-43	24	-24	
6505	-50	35	-48	
6506	-50	30-90	-50	
6507	-51	flat	-51	
6508	-52	50-90	-52	
6509	-52		-52	

2/5/65 & 2/8/65

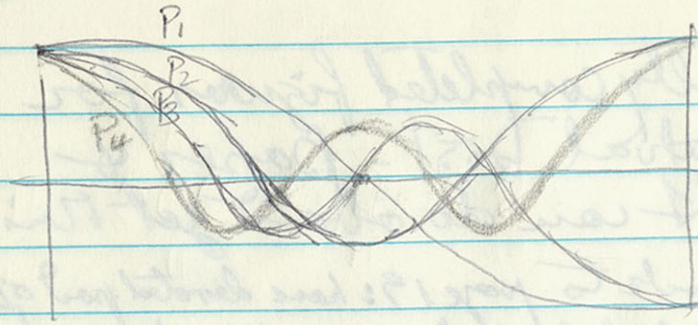
Today noticed the essentially completed figures for the Theoretical Potential Dist - paper & decided to see what I can do about get this paper out also. Refer back to page 19: have devoted part of week to kinetics, but was led to test the advantage of new R_5 + R_6 less constrained than old R_5 (R_3 + R_4) and prepared WXR752C for this. First results promising. Next runs snafued due to someone elses goof at computer; must resubmit

---

2/8/65 WXR752C worked for 6503 – 6509 & some retest of 6501 & 2

Compare Spike Characteristics

	Peak V	at KT	Peak E	at KT	Peak J	at KT	V=0 at KT
6501	.912	26	300	26	70	32	41
6502	.980	25	567	27	64	35	46
6503	.922	25	507	28	269	36	40
6504	.981	25	800	30	328	38	41
6505	.996	26 flat short	1085	33	396	41	44
6506	.997	26 flat long	1395	45	~51	>90	still up at KT = 90
6507	.997	26 flat	1500	51	~90	>90	
6508	.999	28 flat	1591	64	?	>90	
6509	.999	28 flat	1607	87	?	>90	



Therefore lowest order must be P_4 or higher order even term

However Note!, this cancellation occurs only when the three quadrupoles are of exactly the same moment & exactly orthogonal.

Also, when $r \approx l$, have higher order terms as well.

I had not expected this, but it seems that three P_2 fields arranged with orthogonal axes, add up to zero everywhere!

See proof on page 45

2/10

Think about quadrupole field $\psi \propto \frac{P_2}{r^3}$

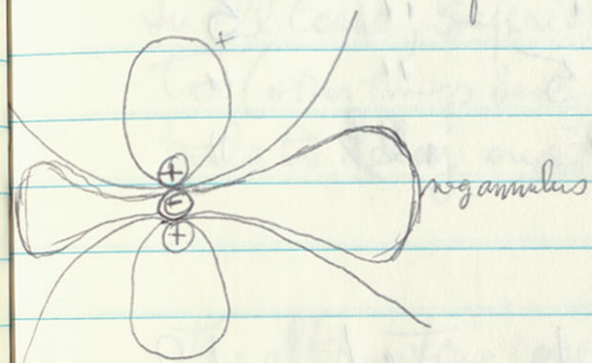
where $P_2(\cos\theta) = \frac{1}{2}(3\cos^2\theta - 1)$

Thus for $\theta = 0$ or π, get $\frac{1}{2}(3-1) = 1$

for $\theta = \frac{\pi}{2}$, get $\frac{1}{2}(0-1) = -\frac{1}{2}$

for $\theta \approx 55°$ or $125°$, get $\frac{1}{2}(1-1) = 0$

$\arccos\sqrt{\frac{1}{3}}$



$\sqrt{.33} = 0.577 \approx 0.58$ for $\cos\theta$

$\therefore \theta \approx 54° 45'$ or ≈ 0.95 radians

Consider three quadrupoles  orthogonally arranged

Along each axis, have $\frac{+1}{r^3}$ due to quadrupole of that axis

and have $2\left(-\frac{1/2}{r^3}\right)$ due to two annuli of other two quadrupoles.

which adds to zero

On on equator get $-\frac{1/2}{r^3}$ from annulus

and if 45° from two poles get $2\left(\frac{+1/4}{r^3}\right)$

0

40°	.38	30°	.625
50°	.12	60°	−.125
	.50		.50

Presumably the points equidistant from three poles are at 54+° where each contributes zero.

$\therefore$ seems to be zero everywhere

note p. 1280 of Morse + Feshbach

New Set-up submitted 2/11/65

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
6502			25	2	1 altered to 6502	.1	10
6511	500	40,000	25	2	.5	.05	10
6512	"	"	"	1	"	"	"
6513	"	"	"	.2	5	.05	10
6514	"	"	"	"	1	.05	10
6515	"	"	"	"	"	"	5
6516	"	"	"	"	.5	"	"
6517	"	"	"	"	3	.03	"
~~6518~~							
~~6519~~							
6521	100	40,000	25	2	1	.1	10
2	200						
3	300						
4	400						
6525	500	40,000	50	2	1	.1	10
6			75				
7			100				
8			150				
9			200				
6531		80,000	25	2	1	.1	10
2		20,000					
3		10,000					
4		5,000					

Anodal try $V = -.7$ with $\mathcal{E} = 400$

$V = -.5$ with $\mathcal{E} = 100$

2/11/65

Attempt to summarize 6501–6509 of WXR752C
See pp. 33, 37, 39

Of these 6502 is probably the best spike
Somewhat similar to older (5) and (7) of WXR751C series

In all cases, superiority rel. to cousins seems attributable to (other things being equal) to smaller value for R_5, which tends to delay onset of J peak, but keeps J peak small. & lets E peak get large.

The alternative cases, like 6503 and very large & later, reduced R_4 makes $\mathcal{E}$ peak later than V peak and these two peaks fall rather closely together. see esp. 6505

6504 & 6505 represent successive reductions of R_5 which delay the growth of J. 6505 is already too flat topped spike.

6506–6509 are all ruled out; first cause is reduced R_6 by factor of 10, which makes J autocatalytic growth occur much too late or not at all.

Could try effect of halving R_6 in 6503 & 6504
→ to become .05 or .5–1

Could also try halving R_7 to 5.

Also try (25, 1, .5, .05, 10)

Anodal: set $J = 0$, set $\mathcal{E} \simeq \frac{R_2}{R_3} V^4 \simeq 1600 \times V^4$

$\cancel{x_1^2+x_2^2+x_3^2}$

$$\cancel{35y^4-30y^2+3}$$

$$\cancel{(5y^2\quad)(7y^2\quad)}$$

$$(35y^2-3)(y^2-1) = 35y^4-38y^2+3$$

$$\therefore 35y^4-30y^2+3 = 8y^2+(35y^2-3)(y^2-1)$$

$$P_4 = \frac{1}{8}\left(35x^4-30x^2+3\right)$$

$$P_4(\theta_1,\theta_2,\theta_3) = \frac{1}{8}\left(35(\gamma_1^4+\gamma_2^4+\gamma_3^4)-30(1)+9\right)$$

$$= \frac{35}{8}(\gamma_1^4+\gamma_2^4+\gamma_3^4) - \frac{21}{8}$$

For $\gamma_1=1$, $\gamma_2=0=\gamma_3$, get $\frac{35-21}{8} = \frac{14}{8} = 1.75$

For $\gamma_1=\gamma_2=\sqrt{2}/2$, $\gamma_3=0$ get $\left(\frac{35}{8}\right)\left(2\left(\frac{4}{16}\right)\right) - \frac{21}{8} = \frac{17.5-\cancel{14}\ 21}{8} = \frac{3.5}{8} = 0.438$

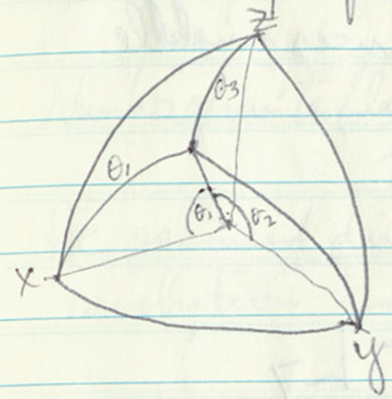
For $\gamma_1+\gamma_2+\gamma_3 = \sqrt{0.333}$ get $\frac{35}{8}(0.333) - \frac{21}{8} = \frac{11.67-21}{8} = -\frac{9.33}{8} = -1.17$

3/9

Perhaps should also consider P_4 term in detail

2/12/65 Refer back to p. 41

Here is proof that $\frac{P_2}{r^3}$ term cancels out for the three orthogonally arranged quadrupoles of equal moment.



Have eight octants of spherical surface. Take an arbitrary point in the octant

~~$\theta_1 = \theta_2 = \theta_3$~~

Note that $P_2(\cos\theta) = \frac{1}{2}(3\cos^2\theta - 1)$

let $\gamma_1 = \cos\theta_1$
$\gamma_2 = \cos\theta_2$
$\gamma_3 = \cos\theta_3$
which also happen to be the directional cosines of the vector in question.

Now, the sum of these three contributions is

$$\frac{1}{2}\left\{3\gamma_1^2 - 1 + 3\gamma_2^2 - 1 + 3\gamma_3^2 - 1\right\}$$

$$= \frac{1}{2}\left\{3(\gamma_1^2 + \gamma_2^2 + \gamma_3^2) - 3\right\}$$

$$= 0$$

because $\gamma_1^2 + \gamma_2^2 + \gamma_3^2 = 1$ identically.

Hence, lowest order term becomes

(see p. 27) $\frac{2ql^2}{4\pi\epsilon}\left(\frac{l^2}{r^5}\right)\left\{P_4(\theta_1) + P_4(\theta_2) + P_4(\theta_3) + \left(\frac{l}{r}\right)^2 (P_6 \text{ etc}\right.$

Count chromatolyzed cells / mm length

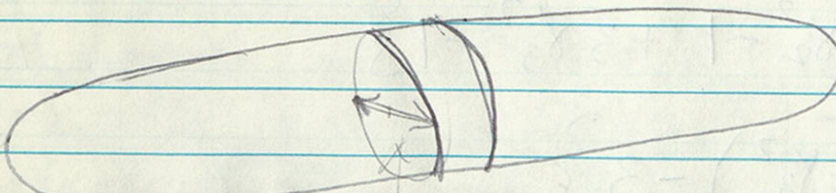
50 40
30/mm near ends   60/mm near middle

Telephone

chromatolysis density $160/mm^3$ at L_7

$\downarrow$ 180μ between cells   from cube root
side of cube

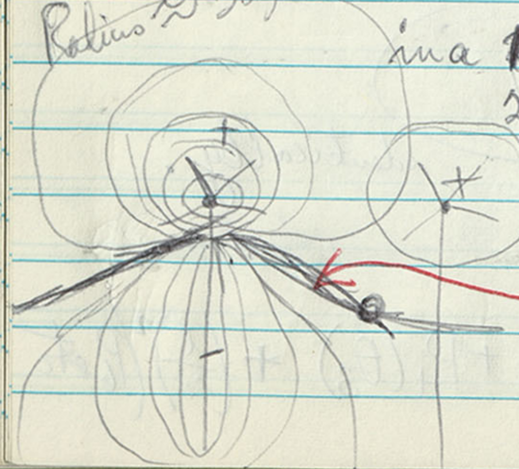
This nucleus contains $630/mm^3$ belong to other muscles.



~~40~~ cross sectional area $.48\ mm^2$

in a 100μ slab, get $.048\ mm^3$ or about 8 cells
200μ slab, get $.096\ mm^3$ or about 16 cells

Radius ≈ 350μ



This shifting zero contour can account for better lateral addition of pos. than for simple dipole.

2/12/65 & 2/15/65

Saw Van Buren on 2/11/65, Phil on 2/12/65

Van Buren found gastroc nucleus about 9.9 mm long
.8 mm dorsoventral
.6 mm lateral

Number of units (large motoneurons)
≈ 370 chromatolysed.

He assumed dimensions to give volume of ellipsoid of revolution and thus got a density of 630/mm^3
for all motoneurons 399 small/ including others grouped

I note that for rectangular parallelopiped, vol ≈ 9.9(.48) ≈ 4.75 mm^3
ellipsoid vol = $\frac{4}{3}\pi ab^2$ where a = major semiaxis & b is minor semiaxis
≈ (4)(4.95)(.123) ≈ 2.44 mm^3

Not sure how this led to his density figure, unless he was including small motoneurons.

He gave average distance between centers as 125 μ from the density figure. Not sure how he got figure, but a rough figure would be $\frac{4}{3}\pi r^3 \approx 4r^3 \approx \frac{1}{2}d^3$

$\therefore d \approx \sqrt[3]{2V}$ where V = vol. per cell.

if vol per cell is $\frac{1}{630}$ mm^3 ≈ 1.6 × 10^6 μ^3
$\therefore d \approx$ ~~1.47 × 10^2~~ ≈ 1.47 × 10^2 μ

but if vol per cell is $\frac{2.44}{370}$ mm^3 = 6.6 × 10^6 μ^3
$\therefore d = \sqrt[3]{13.2 \times 10^6} = 2.36 \times 10^2$ μ

Very roughly, distance over which potentials falls to 10% is 500 μ

Rel magnitudes, in Von Baeren's data

leading pos peak tends to be 0.4 to 0.8 mV

neg peak 1.5 to maybe 3.7 mV

The ratio tends to be in the range $\frac{1}{3}$ to $\frac{1}{5}$

With Phil Nelson's data

max leading ⊕ peak ~ 100μV = 0.1 mV

whereas peak neg is 2 mV or occasionally more

(⊕ peak sometimes greater)

or 1 mV when not very close

∴ Unit ratio ≈ $\frac{1}{10}$ to $\frac{1}{20}$

~~Suppose pos is 0.1 from nearest all~~ e.g.

Possible interp.		Pos	Neg.
nearest unit		0.1 mV	1.2 mV
four next nearest say at	140μ	0.2 mV	0.8 mV
four " "	200μ	0.1	0.4 mV
~~four~~ 8 " "	300μ	0.1	0.1 mV
16	400	0.1	0
		0.6 mV	2.5 mV

see p. 83

Looking with Van Bueren at his prepared figures, I was disappointed not to find the early pos. turn over to neg. at greater depth, as I would have expected for a dipole. But he says he does not actually observe the paths of the axons. (Phil thinks they angle out in caudo-lateral direction) Also, with whole tract, there may be sufficient pos. due to approach of impulse farther down! i.e. when ~~[illegible]~~ near first node, one might expect classical triphasic, except that first nodes are probably not very close together for the population.

Phil's unit data was more hopeful. It did look as if the ⊕ was max slightly dorsal to peak (neg). Also ⊕ seemed smaller as passed peak neg in the ventro-caudal direction: in the "A region" the leading pos. ~~tends~~ tends to get swallowed in A neg. peak & the very slight pos. seen could be due to source phase to approach impulse. Phil thought my idea of relating ⊕ to m spike might work out fairly well, but of course as one moves ~~out~~ along axon, there should always be a brief source phase before sink phase.

Note:

Increments in vol $\propto r_3^3 - r_2^3 \approx r^2 \Delta r$

$\therefore$ equal increments $\qquad \Delta r = \dfrac{\Delta V}{r^2}$

Comments   Anodal break worked o.k., assuming $\mathcal{E} = 100$, $\mathcal{J} = 0$

6511 rel to 6502 has R_5 and R_6 reduced to half.

Main effect was to reduce and delay J peak

* Spike did not return to zero, rose again after dropping to 575

* This might be a model to produce singing

6512 rel to 6511 has R_4 reduced to half. J quenches E less effectively

E peak higher, J peak higher, spike fell to zero at 61

slightly flat topped

6513 rel to 6503 has R_6 reduced to half. This ~~delays~~ decreases J peak

6514 rel to 6504 " " " " " " ; rel to 6513, R_5 reduced to 1/5 This delays J peak

6515 rel to 6514, R_7 is halved. got J peak larger & more prolonged

6516 rel to 6515, R_5 is halved.

6517 rel to 6516, R_6 is reduced

6521 — 6524 reducing R_1 had very little effect.

6525 — 6529 increasing R_3 reduces and delays E peak

" " " V peak

" " " J peak

6531 R_2 increased, faster spike

6532-34 R_2 decreased, slower spike

6526 is very similar to 6532

6532 with $R_2 = 20 \times 10^3$ looks rather good slower spike

2/15/65 6511 – 6534 with WXR752C

see pp 42–43 & 39

	Peak V	@ KT	Peak Ed	KT	Peak Jd	KT	V=0 KT
6511	.990	26	730	29	45.5	42	—
x 6512	.990	26	827	30	73	42	61
6513	.928	25	553	29	203	37	45
* 6514	.983	25	890	31	204	42	52
6515	.982	25	874	31	239	43	48
6516	.990	26	990	32	244	45	50
* 6517	.990	26	1048	34	179	50	60
6521	.979	27	560	29	64	37	48
6522	.980	27	565	29	64	37	48
6523	.980	26	565	28	64	36	47
6524	.980	26	567	28	64	35	46
6525	.978	31	448	33	50	42	58
x 6526	.975	38	362	39	40	51	73
6527	.972	46	298	47	33	61	>90
6528	.967	66	213	67	23.7	85	>>90
6529		>90		>90		>90	>>90
* 6531	.984	17	937	19	103	25	30
* 6532	.972	36	339	39	39	50	78
6533	.962	51	198	54	23	69	>90
6534	.947	70	114	73	~13	>90	>90

Compare $\dot{\mathcal{E}} = R_1 V^2 + R_2 V^4 - (R_3 + R_4 J)\mathcal{E}$

in 6502, 6513 } at first at KT = 35 and KT = 40

		V	$\mathcal{E}$	J	$\mathcal{E}J$	$R_4\mathcal{E}J$	$R_3\mathcal{E}$
6502	KT=35	.629	86.55	64.22	55×10^2	110×10^2	21×10^2
	KT=40	.240	7.57	55.34	420	840	190
6513	KT=34	.621	314.54	183.18	576×10^2 5.8×10^4	115×10^2	78×10^2
	35	.551	250.7	194			
	40	.199	58.54	195	114×10^2	23×10^2	16.5×10^2
	39	.260	80	199	160×10^2	32×10^2	

$$\dot{V} = -V + (1-V)\mathcal{E} - (V+.1)J$$

Compare $(.37)86 - (.73)64 = 32 - 47 = -15$

with $(.37)(315) - (.73)(183) = 116 - 134 = -18$

similar

Compare $(.75)(7.6) - (.35)(55) = 5.7 - 19.3 = -13.6$

with $(.75)(80) - (.35)(200) = 60 - 70 = -10$

similar

In 6502, the $(1-V)\mathcal{E}$ terms drops by factor 5.6, and the $(V+.1)J$ by 2.07

In 6513 .... 1.93, ... 1.91

2/16/65 General Comments upon 6501–6534

6502 and 6532 maybe the two best spikes, differ by only a factor of 2
faster slower in value of R_2

It is interesting that 6502, 6513 and 6521 have very similar spikes even though the E + J peaks are rather different. This is worth looking into

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
6502	500	40,000	25	2	1	.1	10
6513	"	"	"	.2	5	.05	10
6521	100	"	"	2	1	.1	10

Actually 6521 is essentially the same as 6502, but 6524 is even closer.

* But with 6502 & 6521–24

$V_{peak} =$ .980 at 25 $E_{peak} \simeq$ 567 at 27 $J_{peak} \simeq$ 64 at 35

whereas with 6513

.928 25 553 at 29 203 at 37

i.e. J peak is three times as large a little later
at KT = 35 it is 194. almost exactly 3 times

Apparently tripled J with $\frac{R_4}{10}$ reduces E quench by that amount which compensates for tripled V quench.
(Note at left that $R_4 E J$ is almost the same at KT ≈ 34, 35)

This can be seen approx by looking at already plotted curves of E & J in 6502 & 6503, where 6503 is better than 6503 because R_6 was halved.

i.e. in 6502 E is quenched faster than V

6514 worse because R_5 too small

Actually, 6513 is better than 6514
as a case of strong overlap of E & J

Make KHVSD = 1

~~New runs~~
6513 with initial voltage at .005, .10, .15
6502 " " " " " "
~~6532 for longer time~~
both of above for NT = 150 with KHVSD = 1

6532 like 6502 with R_2 = 20,000
6543 ~~with~~ like 6513 with R_2 = 20,000 also
~~[illegible]~~

also 6521 for thresholds

	R_1	R_2	R_3	R_4	R_5	R_6	R_7
6532	500	20,000	25	2.0	1	.1	10
6543	500	20,000	25	.2	5	.05	10

2/16/65

It is tempting to try for a curve between 6513 & 6514 but not necessary

Try with $R_5 = 2.5$

also $R_4 = 1$ or 0.5

This should avoid delaying J as much as in 6514

but make it a little later than in 6513

The importance of $R_4 = 0.2$ is that this permits larger J and E, which works well only if J is slightly more delayed, and V falls with E

Looking at page 52 comparing 6502 ($R_4 = 2$) with 6513 ($R_4 = .2$) it is clear that 6513 obtains falling V by ~~[illegible]~~ opposing effects of large E and J, wheras 6502 does this with differencing smaller E & J effects.

It happens that $(1-V)E$ and $(V+.1)J$ both fall roughly to half for 6513 from $KT = 35$ to 40

J itself is nearly constant, while E goes to 1/4.

but $(1-V)$ doubles and $(V+.1)$ halves.

Should run 6532 for a longer time

Also run mod. of 6513 with $R_2 = 20{,}000$

Interesting to compare thresholds of 6513 & 6502 & also propagation safety factor, which could be handled by $\mu_{ij} = \alpha \mu_{ji}$

Already tried anodal initial condition $V = -.5$, $\varepsilon = 100$ which worked well

Now can try ~~$V = -.25$, $\varepsilon = 25$~~

$\varepsilon = 25$, $V = -.35$

$\varepsilon = 50$, $V = \left(\frac{1}{2}\right)^{1/4}(-.5) = (.84)(-.5) = -.42$

2/16/65

With regard to anodal applied current st. st.

For any applied current st. st. have

$$\psi = V - (1-V)\mathcal{E} + (V-\beta) j$$

or $$\frac{\psi}{V} = 1 - \left(\frac{1-V}{V}\right)\mathcal{E} + \left(\frac{V-\beta}{V}\right) j$$

Now, for anodal st. st., assume $j = 0$

and $y = -V$, is a positive quantity

Then $$\frac{\psi}{V} = 1 + \left(\frac{y+1}{y}\right)\mathcal{E} \quad + \frac{y+\beta}{y} j$$

Now, if $\mathcal{E}_{stst} = \frac{R_2}{R_3} V^4$, get $1 + \frac{R_2}{R_3}(y^3 + y^4)$

whereas if $\mathcal{E}_{stst} = \frac{R_1}{R_3} V^2$, get $1 + \frac{R_1}{R_3}(y^2 + y)$

$\frac{R_1}{R_3} \simeq \frac{500}{25} = 20$, if $y = 0.1$, get $1 + 2.2 = 3.2$

$\frac{R_2}{R_3} \simeq \frac{40,000}{25} = 1600$, if $y = 0.1$, get $1 + \underbrace{(1600)(.0011)}_{1.76} \simeq 2.76$

6802 with $V = .05$ at $KT = 90$

for $V = .05$, $V^2 = .0025$, $R_1 V^2 = \frac{500}{400} = 1.25$

$V^4 = \frac{1}{16 \times 10^4}$, $R_2 V^4 = \frac{4 \times 10^4}{16 \times 10^4} = \underline{\underline{0.25}}$

$\therefore R_1 V^2 + R_2 V^4 = 1.50$

whereas $-R_3 \mathcal{E} = (-25.)(.059) \approx -\frac{6}{4} = -1.5$ ✓

$\mathcal{E} g \approx 36 \times 10^{-5}$, $\therefore R_4 \mathcal{E} g \approx 10^{-3}$

also $\tau \dot{V} = -V + (1-V)\mathcal{E} - (V+.1) g$
$= -.05 + (.95)(.059) - (.15)(.006)$
$= -.050 + .056 - .0009$

whereas for 6513 $V = .049$, $\mathcal{E} = .056$, $g = .028$, $\mathcal{E} g = .0016$
$R_4 \mathcal{E} g \approx .008$

$-R_3 \mathcal{E} = (-25.)(.056) \doteq 1.4$
$-R_3 \mathcal{E} - R_4 \mathcal{E} g \approx -1.48$

also $\tau \dot{V} \doteq -.05 + (.95)(.056) - (.15)(.028)$
$\doteq -.05 + .05\cancel{4} - .0042$ close.

Note that if $V \ll 1$ $\frac{1}{V(1-V)} \approx \frac{1}{V}$ and $\frac{R_1 + R_2 V^2}{R_3} \approx \frac{R_1}{R_3}$

giving $V \approx \frac{R_3}{R_1}$

Since $V = \frac{R_3}{(1-V)(R_1 + R_2 V^2)} = \frac{R_3}{R_1 \left(1 - V + \frac{R_2}{R_1}(V^2 - V^3)\right)}$ see p. 58

2/18/65

Got back new 6502–6543 series (WXR 752C) testing threshold, anodal break etc.

interesting that 6502 ($R_1=500$) threshold is $V=.05$

whereas 6521 ($R_1=100$) threshold $>V=.05$
$<V=.1$

So some very slow subthresholds, may need to reexamine with larger NT ~~and~~ DT and NSTEP.

General analysis – We can estimate threshold condition with $\dot{V}=0=\dot{\mathcal{E}}$ and J small

$\dot{\mathcal{E}}=0$ means $\mathcal{E}=\dfrac{R_1V^2+R_2V^4}{R_3+R_4J}$

$\dot{V}=0$ means $\mathcal{E}=\dfrac{V+J(V+.1)-\psi}{1-V}$ See p. 35

For $\psi=0$ and $J=0$, we get simply

$$\mathcal{E}\approx\frac{V}{1-V}=\frac{R_1V^2+R_2V^4}{R_3}$$

Dividing through by V^2 we get the interesting requirement.

$$\frac{\mathcal{E}}{V^2}\approx\frac{1}{V(1-V)}=\frac{R_1+R_2V^2}{R_3}$$

which could be plotted as an intersection, where the roles of R_1, R_2, R_3 can be easily distinguished.

From $\frac{1}{V(1-V)} = \frac{R_1 \cancel{} + R_2V^2}{R_3}$

we can say that $V^* = \frac{R_3}{R_1(1-V)(1+\frac{R_2}{R_1}V^2)}$

$\therefore V^* < \frac{R_3}{R_1}$ whenever $\left(1+\frac{R_2}{R_1}V^2\right) > \frac{1}{1-V}$

$(1-V)^{-1} = 1+V+V^2+V^3 \ldots$

i.e. want $\frac{R_2}{R_1} > \frac{V+V^2+V^3, \ldots}{V^2}$

see opposite

If $\mathcal{E}_{st} = .06$, then $J_{st} \simeq \left(\frac{1}{10}\right)(.06) = .006$ which is correct

Whereas $\mathcal{E}_{st.} = \frac{V}{1-V} = \frac{.05}{.95} = .0525$

J_{est} from $\mathcal{E}_{est.} = .00525$

Then $J(V-\beta) = J(.15) \simeq .0008$

and $\alpha = \frac{.0008}{.05} = .016$

checks

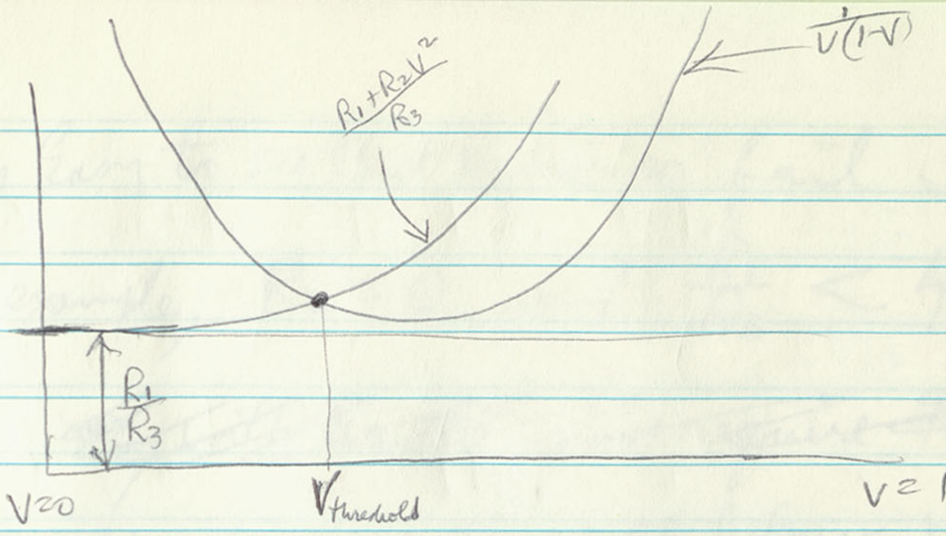
For 6502, $\alpha \approx \left(\frac{1}{10}\right)\left(\frac{.05+.1}{\cancel{}(.95)}\right) = \frac{.15}{\cancel{}\ 9.5} = .0157$

$\approx .016$

Neglect of $R_4 J$ ~~and α~~ causes only 10^{-3} error factor

Neglect of α causes 1.6×10^{-2} error factor i.e. 1.6%

2/18/65



To restore finite J to analysis, we can do this first to get $V_{estimate}$

then $\mathcal{E}_{estimate} = \frac{V}{1-V}$

and $\dot{J}=0$ would give $J_{estimate}$ from

$$J = \frac{R_5 \mathcal{E}}{R_7 - R_6\mathcal{E}} \approx \frac{R_5}{R_7}\mathcal{E}$$ when $R_6\mathcal{E} \ll R_7$

now, using this J, we can examine the following

$$\frac{1+\alpha}{V(1-V)} = \frac{R_1 + R_2 V^2}{R_3 + R_4 J}$$

where $\alpha = J(V-\beta)/V$ where $\beta = -.1$ in these examples

$$\approx \left(\frac{R_5}{R_7}\right)\left(\frac{V}{1-V}\right)\left(\frac{V+.1}{V}\right)$$

$$= \left(\frac{R_5}{R_7}\right)\left(\frac{V+.1}{(1-V)}\right)$$

for $\Psi \neq 0$

α has also $-\frac{\Psi}{V}$

2/18/65

∴ Easy to see that kinetics fail when, for example, $R_2 = 0$ and $\frac{R_1}{R_3} < 4$

~~Or, with $R_2 \neq 0$, we require that~~

Also, if we require threshold below $V = 0.5$

Then we can require $\frac{R_1 + R_2 V^2}{R_3} > 4$ for $V = 0.5$

or $R_2 > \frac{4R_3 - R_1}{.25}$

or $R_2 > 4(4R_3 - R_1)$

or $\frac{R_2}{R_3} > 16 - 4\frac{R_1}{R_3}$

If want threshold at $V = 0.1$

Then must have $\frac{R_1 + 0.01R_2}{R_3} > \frac{1}{.09} = 11.11$

R_1	R_2	R_3	R_4	R_5	R_6	R_7	
.5+3	.1 neglig.	.2+2	.1-4 neglig.	.2+1	.1-5 neglig.	.1+2	6551
"	"	.1+2	"	"	"	"	6552
"	"	"	"	.5+1	"	"	6553
"	"	"	"	"	"	.5+1	6554

Now restore R_2 but leave out R_4 & R_6

.5+3	.2+5	.25+2	.1-4	.5+1	.1-5	.1+2	6555
"	"	"	"	.1+2	"	"	6556
"	.2+4	"	"	"	"	"	6557
"	"	"	"	"	.1-0	"	6558
"	"	"	.1+1	"	.1-5	"	6559

Thresholds ~~6560~~

.5-2	.4+5	.25+2	.2+1	.1+1	.1	.1+2	6560

Try with NT=90, DT=.02, NSTEP=10, V= .15, ~~.11~~, .10, ~~.09~~, ~~.08~~

V .07

6502 with (.06, .05, .04, .03)

6521 with (.11, .10, .09, .08, .07, .06)

2/18/65

Check over runs & plan more if necessary to see how well can work with R_2, R_4 and $R_6 = 0$

believe it will work, but be limited.

R_2 adds steepness to spike without hurting threshold too much.

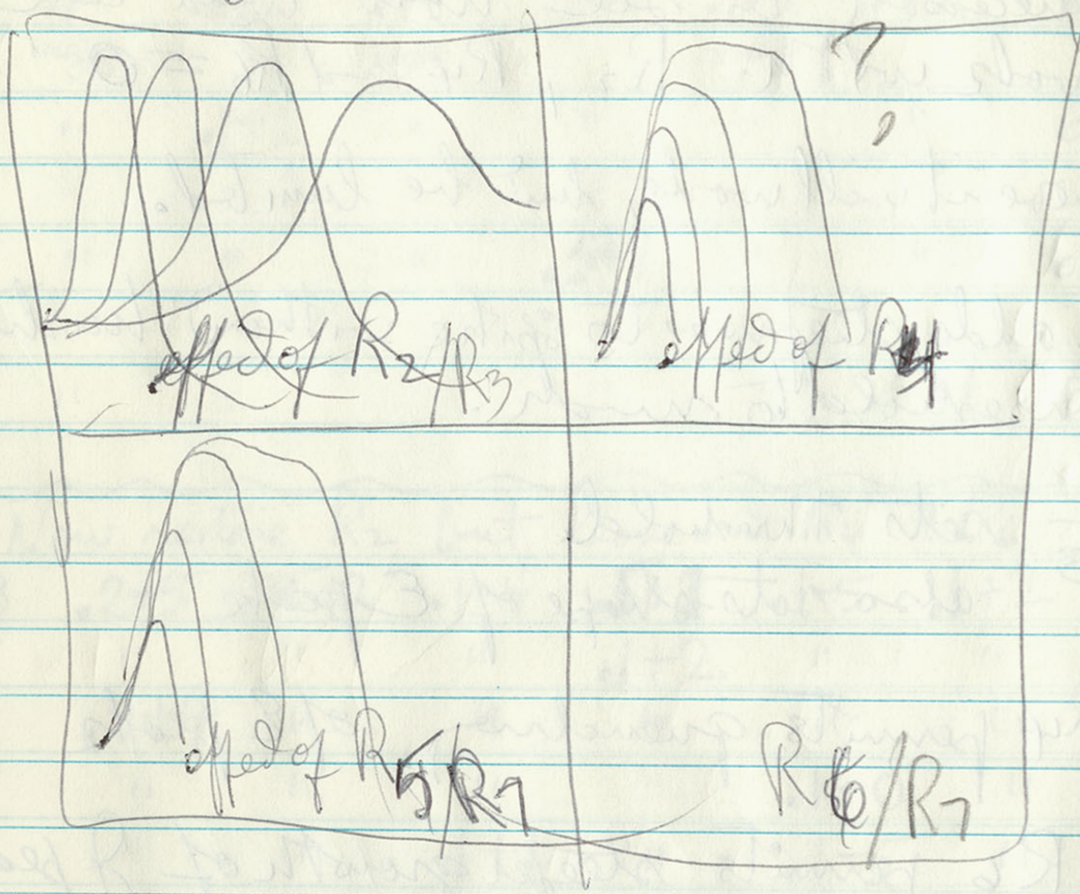
$\frac{R_1}{R_3}$ sets threshold
also sets shape of E peak.

adding R_4 permits quenching of E peak

adding R_6 permits steeper growth of J peak
6506–6509 attest to need for R_6 & R_4

6534 provides some evidence on R_2

Plan Fig. 2



4000 series related to 6503

5000 series related to 6513 & 6514

6000 series related to 6504

7000 series related to

Need R_4 increased to ~~10~~ 5 & 10 and reduced to ~~.05~~ .10 to complete 6502, 6504 pair

Need R_6 = .5 and 1 ~~& 2 ohm~~ to complete 6504, 6514 pair

2/24/64 wrote part of manuscript ~~for~~ fraction pd paper yesterday. Planning figures today.

Fig. 1-A (6543) has (relative of 6513)
500, 20,000, 25, 0.2, 5, 0.05, 10

v peak = .901
ε peak = 298.7
J peak = 108.6

$\frac{J\text{ peak}}{\varepsilon\text{ peak}} = 0.364$
$> 1/3$

Fig. 1-B (6532)
500, 20,000, 25, 2.0, 1, 0.1, 10

v peak = .972
ε = 338.9
J = 38.74

$\frac{J\text{ peak}}{\varepsilon\text{ peak}} = 0.114_3$
$< 1/8$

Plan 6531, 6502, 6532, 6533 series on R_2
80,000, 40,000, 20,000, 10,000

Must run a new series on R_4 starting with 6532
want R_4 = ~~8, 4, 2, 0.5, 0.2~~
10, 5, 0.2, 0.1

Also, series on R_5, using 6513 (5) & 6514 (1) or 6503 – 6505
add the cases R_5 = 10, 0.5, 0.2, 0.1

Series on ~~R~~ also starting with 6532, add cases R_5 =

			V
6502 threshold series	showed very slight local resp for		.03
	a little more		.04
	bordyn? above thresh		.05
	spiked	T = 1.1	.06
		0.74	.07
		0.37	.1
		0.19	.15
		0.125	.20

6521 threshold	nearly passive for		.05
	slight local		.06
	slightly more "		.07
	" " but still decay		.08
	above thresh – spiked	T = .9	.09
		~ .6	.10
	Make a figure of this	~ .44	.11
		.225	.15
		.135	.20

2/25/65

Refer back to p. 64 for testing small R_2, R_4, R_6

6551 builds rather slowly. try increasing R_1 to $.5 \times 10^4$
~~R_3 to $.2 \times 10^3$~~
R_5 (?)

try 6561

6562 with $.1 \times 10^5$

6552 built E larger because of smaller R_3, but still too slow

6553 larger R_5 built J to large rel to E

6554 smaller R_7 " " " " " "

6555 $R_2 = 20,000$ produced spike which falls very slowly.

try larger R_5 & smaller R_7

.1 + 2 .5 + 1

6556 in fact did this and worked ~~fairly~~ well

good

should plot

6557 reduced R_2 by factor of 10, not very good

6558 $R_6 = 0.1$ had little effect on early part, as might be expected.

Note: 6556 is a good spike with $R_4 = 0 = R_6$

6561 may lead to one with R_2 also zero ?

This output missing after Calif. trip. I believe many of these notations were on this output.

In 4000 series

R_4 from zero thru 0.1

had essentially no effect upon the rising phase of the spike, or upon E and J thru KT = 25

~~other~~ smaller E & J become significant only for KT > 26

obviously at E & J peaks

Also, note v peak earlier than E peak for $R_4 < 5.$
" plots of " later " " $R_4 > 5.$

Perhaps compare 4005 with 4000

or maybe 4000, 4004,

Do 4008 with $R_4 = 1$

? Also do another series like 4000 series ($R_6 = .1$)
for which $R_6 = 0$

? Also might try smaller R_3
with proportionately smaller R_1 & R_2

The largest effect is in J peak amplitude

Zero KT	R_4
44	0
43	.01
41	.05
40	.1
39	.5
47	5
63	10
>90	20

apparently J too small
i.e. R_7 too big

2/26/65 Analysis of series 4000 — 7000

Related to 6503

Series 4000 varied R_4 from zero to 20.
This documents what was already learned from 6556.
Namely, that with R_4 zero, J cannot pull E down directly & thus J builds up larger & pulls v down & hence E down, whereas, when R_4 is large, J never gets very large because it pulls E down & it is the drop of E, not the J which pulls v down.

The effect of R_4 zero could be exaggerated with smaller R_3 also (ie. smaller self-decay) as in case of 6503

In the 4000 Series

R_1	R_2	R_3	.2	R_5	R_6	R_7
500	40,000	25		5	.1	10

~~4000~~	Vpeak	at KT	Epeak	at KT	Jpeak	at KT
~~4000~~	~~.921~~	~~25~~	~~435~~	~~27~~	~~159~~	~~34~~
4000	.924	25	606	30	1351	47
4001	"	"	596	29	962	43
4002	.923	"	571	"	546	39
4003	. "	"	543	"	390	37
4004	.921	"	435	27	159	34
4005	.901	26	208	26	40	32
4006	.878	27	139	26	27	33
4007	.838	29	83	27	18	35
4008	.917	25	374	27	105.	33

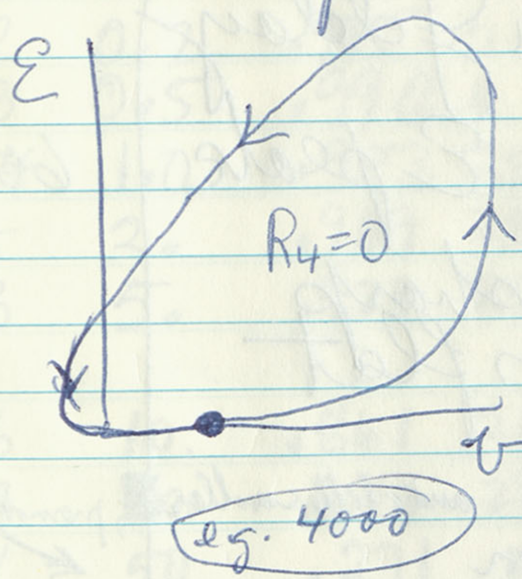
2/26/65

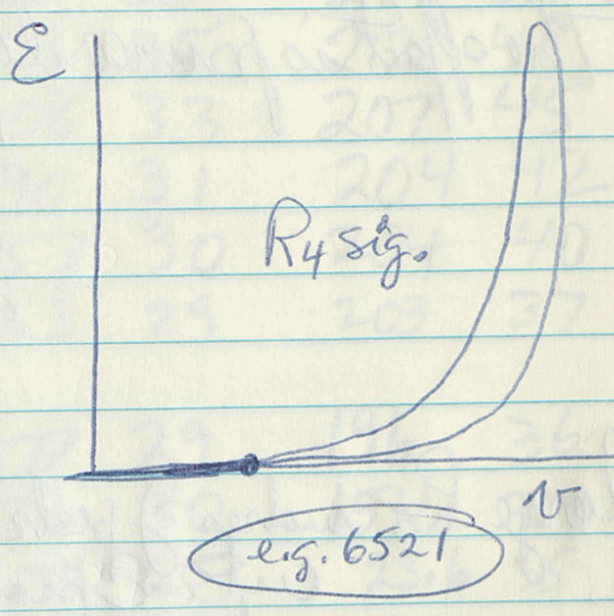
Discussion of $R_4 = 0$ versus R_4 large.

Have now shown that can get good spike either way.
When $R_4 = 0$, J pulls down v and v pulls down $\mathcal{E}$
When R_4 large, J pulls down $\mathcal{E}$ and $\mathcal{E}$ pulls down v

However, voltage clamping experiments require a significant R_4 term to pull $\mathcal{E}$ down.

Note $\mathcal{E}$ vs v plots





Will make figure

Still need 5006 with $R_5 = 10.$
7 20.
8 50.

$$J^* = \frac{R_5 E - \cancel{R_6 E}}{R_7 - R_6 E}$$

Note that J peak amplitude is remarkably similar

* The effect is primarily upon J delay
E peak
& V sharp or flat

6514 =

large R_5 makes J peak earlier and a little smaller, presumably because
cuts E peak down
cuts V peak down

small R_5 makes J peak later
lets E peak get larger + later
lets V become flat topped

2/26/65

Took at 5000 series, related to 6513 & 6514

R_1	R_2	R_3	R_4	R_5	R_6	R_7
500	40000	25	.2		.05	10

Obviously $R_5 = 0$ keeps $J = 0$ & we have reduced problem ~~of~~ going to permanently ~~on~~.

5001 had $R_5 = 0.1$ get flat top spike

~~#~~	R_5	vpeak at		Epeak at		Jpeak at		K_5 zero
5001	0.1	.997	26	1222	36	217	50	59
5002	0.2	.995	"	1139	35	212	48	57
5003	0.5	.990	"	1008	33	207	45	54
5004	1.0	.983	25	890	31	204	42	52
5005	2.	.969	25	757	30	204	40	49
6513	5.	.928	25	553	29	203	37	45
5006	10.	.861	26	377	29	196	36	43
7	20.	.699	28	173	30	154	37	44
8	50.	.271	20	7.74	25	23.6	35	52

2/24/65

Look at 6000 series, related to 6504

R_1	R_2	R_3	R_4	R_5	R_6	R_7
500	40,000	25	.2	1.		10

Epeak = 1038

6000 was underquenched Jpeak = 70

larger R_4 or R_5 would probably correct this

6504 had R_6 = .1, then Epeak ≈ 800 Jpeak ≈ 330

6001 .2 688 552

6002 .5 very rapid fall of V

~~turnover at 34~~

→ Jpeak twice Epeak

6003 1.0 Jpeak 4x Epeak

6004 & 6005 terribly abrupt fall o/v

Conclusion is that large R_6 can be used only if R_5 and R_4 are smaller.

Not sure that R_6 is necessary. Its only important purpose would be that if we want to use a small R_5 to obtain delay, and yet build up to a large peak, can then use R_6 for this.

e.g. if want J to effect V more than E, make R_6 larger & R_4 smaller
" " " " E more than V, " " smaller & R_4 larger

Could try 7005 with $R_7 = 20$

Turned out not underquenched i.e. OK

2/26/65 Look at 7000 series, related to 6504 & hence to 6000 series

7000 with $R_7 = 0$, J rises to permanent plateau. But effect is small up to spike peak

7004 with $R_7 = 50$ was underquenched (oscillatory spike)
$R_7 = 20$ was OK

7003 with $R_7 = 5$ spike fell very slightly more rapidly than 6504

7002 with $R_7 = 1$ spike falls a little more rapidly. J remains large

7001 with $R_7 = 0.1$ spike falls a little more rapidly J remains up much too long

* i.e. set R_7 for refractory period
then set R_5/R_7 and R_6/R_7 for J peak
for J delay

6570 series

~~& smaller~~ R_7

Definitely try smaller R_3 with smaller R_1 & R_2

	R_1	R_2	R_3	R_4	R_5	R_6	R_7	
0	200	8,000	10	2	1	.1	10	like 6532
1	"	"	"	.2	5	.05	10	like 6543
2	100	4,000	5	2	1	.1	10	
3	"	"	"	.2	5	.05	10	

Call these 6570, 1, 2, 3 also try

4	100	4,000	5	0	10	0	10
5	"	"	"	"	20	"	"
6	"	"	"	5	5	0	10
7				10	5	0	10
8				5	10	0	10
9				10	10	0	10

Results 3/2/65 with modified order

2/26/65

see p. 69 for setting up

These all have $R_4 = 0 = R_6$

6556 rerun with DT = .01, NSTEP = 5

6561 like 6551 with $R_1 = .5 \times 10^4$ — By mistake R_5 too small

6563 " " " " $.1 \times 10^5$

6562 " 6552 $R_1 = .5 \times 10^4$

6564 ~~~ $.1 \times 10^5$

6566 like 6556 with $R_2 = .4 \times 10^5$ O.K.

6567 " with $R_2 = 0$, $R_1 = .5 \times 10^4$ oscillates

6568 " " $R_1 = .1 \times 10^5$ oscillates

Also setup

7005 with $R_7 = 20$

4008 with $R_4 = 1$

5006 $R_5 = 10.$

5007 20.

5008 50.

also one with KHVSD = 1

Also do 6521 with I.C. $v = .4$

.6

.8

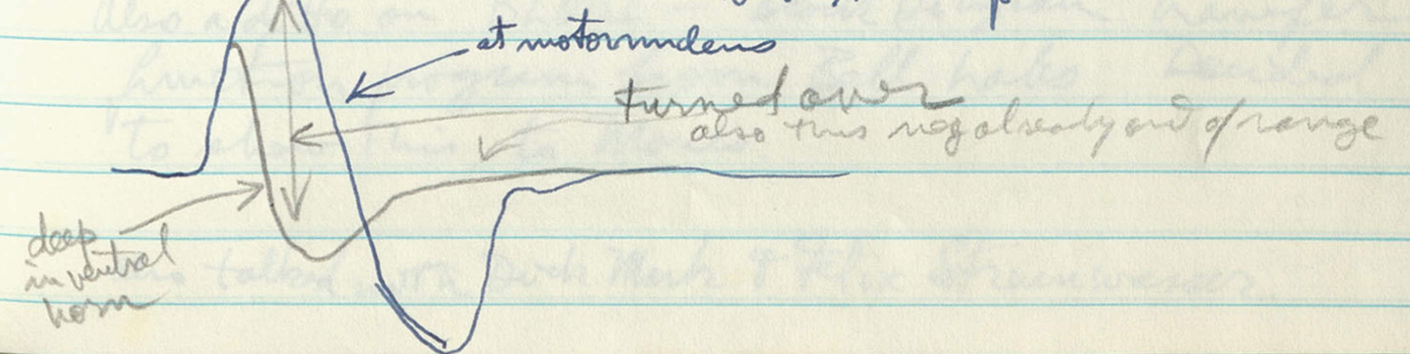
3/2/65 Today, concentrate on preparing notes for Cal. Tech lectures 3/5 and 3/8

Because sent reprints (Ojai + two Exp. Neurol.), ~~but~~ in place of course notes, best plan is to base lectures upon these reprints and esp., upon the equations and figures contained in these reprints.

Also, can prepare ditto's of any supplementary equations, which dittos can be run off at Cal. Tech.

∴ Lecture I — to be based on Ojai reprint.
~~Lecture~~ Lecture II — to pick up bases + est. of params.
(see p G.H.I [of this notebook] earlier + also abstracts sent Fender

* Phil Nelson sent over tracings showing that the dipole aspect for single motoneuron leading pos. is pretty well maintained by going deeper. (i.e. there still a little early ⊕ presumably due to more distant sinks in axon but main part turns over.



Telephoned Fashel, but it was difficult to arrange a meeting, esp. with him & Moore of Segundo. Ended up postponing this. May see them at Gordon Conference.

Then it turned out that I did spend a few hours at UCLA because Fender drove me over when he went to see Bullock and Thorson

3/12/65

Returned from Cal. Tech trip.

Lecture I was probably O.K.

Lecture II not thoroughly prepared. Too much jumping around, although this was of interest to some students.

But I came to realize that for a course, a lecture probably should plod more slowly and carefully through the essential details than I have become accustomed too for seminars etc.

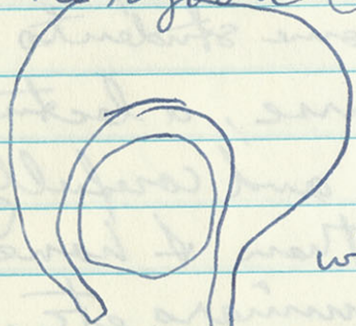
* The students ~~should~~ should be able to produce a coherent set of notes from the lecture. Easiest, of course, if one provides them with ditto outline or notes, which can be prepared by hand.

They gave me a ditto by Benson, McCann & Taylor, for using the Perkel program for neural network modeling, but talking with Fender also brought out some of the basic difficulties of the Perkel program. Perkel focuses on "time of firing" and uses instantaneous voltage changes partly for convenience: if it is above threshold, time of firing is given immediately. Threshold recovery is treated as a simple exponential.

Also a ditto on BLODI — Block Diagram transfer function program from Bell Labs. Decided to show this to Manes.

also talked with Dick Mark & Felix Strumwasser

Tom Reese also observed some peculiar cupping of neurons, in ~~the region~~ (satellites) surrounding glomeruli.



with synapses on the outer cell

He is Pondering what function this could have?

companion
maybe ~~jointly~~ with a ~~paper~~ by ~~Reese~~ on his ~~anatomy~~.
two or three

Maybe we should try to write a short note with three authors, pointing out that we are combining several distinct sources of information

(1) Waves vs time & depth

(2) ~~Interp as~~ extracell current flow

(3) joint facts of (a) Period III orientation

(b) Period III mitral J

Book 4, p. 57 (8/24/64) (c) Consequent granule implication

~~(d)~~ requiring granule dendritic depolarization.

(4) ∴ postulate E from mitral sec to granule dendrites.

slow fizzle response

during which J from granule dendrites to mitral sec.

(5) Tom Reese has now observed such synapses.

3/15/65

Attended Tom Reese's 9:00 AM lecture on histology of Olfactory Bulb. The most important point for me and Gordon is that he has now observed several cases that look like synapses from mitral secondary dendrites to neighboring structures which could very likely be spines (gemmules) of granule cell dendrites. After this seminar Tom came over to my office to learn what Gordon and I had been postulating about dendrodendritic synapses between mitral secondaries and granule dendrites. The orientation of a synapse seems to be fairly widely accepted as having the vesicles clustered on the presynaptic side, and some sort of a lattice-like apparatus (can't recall the word just now — web) on the postsynaptic side, extending intracellularly from the dense post-synaptic membrane. What this synapse does is to provide the means of mitral activity inducing granule dendritic depol., which we ~~feel~~ are almost compelled to assume from the field considerations. The rest of the story still requires the slow, fizzling response of granule dendrites ~~with~~ which will be presumed to exert an inhibitory effect upon the mitral cells, in a wide lateral inhibitory sense. This inhibition could conceivably be by means of very special synapses, but it could perhaps more simply be by means of ordinary inhibitory synapses, with sustained effect due to fizzly character of granule cell response. The collaterals from mitrals to granule cell bodies would have to be inhibitory. This is the same idea that Gordon & I had earlier, but we did not have the fact of such synapses having been observed.

3/16/65 3/17/65

Spent afternoon with K. Frank, Phil Nelson, Bob Burke, and Ted Evans (from Birmingham) regarding Tom Smith's conclusions & arguments, as now incorporated in a manuscript. Also discussed some of Bob Burke's observations of epsp and ipsp shapes & interactions. Question to consider is which computations that I could perform would be the most useful in checking out the various questions that bother them.

K. Frank especially concerned about question that he & I & Phil & Tom discussed numerous times. How detectable at the soma is a dendritic conductance change which generates a significant epsp. Is it possible to generate a sig. epsp at soma & still have the conductance change measurement be close to noise? K thought my case of chopping off dendrites at different lengths might be O.K., but even then, I think I had to treat the conductance change as const, not brief. This would only set an upper limit, but can do for different frequencies. Computationally, I can have ε be brief, but easier to apply step than to apply A.C. – but could even try that too.

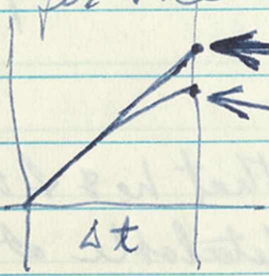
Computations — phase sensitive detection T.G. Smith & J.S. Bryan

(1) After reading Tom's phase methods (for 100 cps), decide if it would be fruitful to set up computation for peripheral ε with applied + & – current step at soma.

(2) Consider extension to A.C.

Note, with regard to single lump story, we have the problem that epsp peak non-linearity lies between (1) linearity of initial slope
(2) non-linearity of st.-st.

But, given Δt, this can be made quantitative for the single lump.



$$\Delta t\, \dot{v}_0 = \frac{\Delta t}{\tau}\left\{(1-v_0)\Delta\varepsilon - (v_0-\beta)\Delta j + \Delta\psi\right\}$$

$$\frac{\tau \dot{v}_0}{\mu\tau}\left(1-e^{-\mu\Delta t}\right)$$

$$\text{Ratio} = \frac{v(\Delta t) - v(0)}{\Delta t\, \dot{v}_0}$$

$$= \frac{(v_s - v_0)\left(1-e^{-\mu\Delta t}\right)}{\Delta t\, \dot{v}_0}$$

and eq (12) of Ojai gives $v_s - v_{0s} = \frac{\tau \dot{v}_0}{\mu\tau}$

$$= \frac{1-e^{-(1+\varepsilon+j)\Delta T}}{(1+\varepsilon+j)\Delta T}$$

If $(1+\varepsilon+j)\Delta T = x$

~~Hence~~, $\text{Ratio} = \frac{1-e^{-x}}{x} = \frac{1-1+x-\frac{x^2}{2!}+\frac{x^3}{3!}-\frac{x^4}{4!}+\cdots}{x}$

$$= 1 - \frac{x}{2!} + \frac{x^2}{3!} - \frac{x^3}{4!} + \text{etc}$$

which is useful when x is small

The interesting point is that ψ, v_0, β etc. all wash out. But, of course

3/17/65

(3) Re Bob Burke's interaction, would like more dramatic theoretical demonstrations of occlusive & non-occlusive types of interaction. epsp about 3 to 4 mV apiece

Try to get some linear to within 1%

others losing as much as 15%

Also, with sensitivity to timing.

i.e. (A) simultaneous epsps (as seen)

(B) shifted in both directions

Note: the more peripheral one should be made stronger to match better.

I may be able to heighten some effects by using larger $\mathcal{E}$ in single compartments.

Consider	$\mathcal{E} = \cancel{4}$ in cpt. 3 or 2	$\mathcal{E} = 5$
and perhaps	$\mathcal{E} = \cancel{8}$ in cpt 5 or 4	$\mathcal{E} = 10$
" "	$\cancel{16}$ in 7 or 6	$\mathcal{E} = 20$

Also, consider J ten times $\mathcal{E}$

At the other extreme, use small $\mathcal{E}$ over large area

effects of changing V in neighboring cpts. won't wash out this way. Might take up with Zim.

See p. 94

	65.101	1.	-.1		ordinate scale set
		1.	.35		
		1.	gives baseline at T=0		During $\mathcal{E}=5$ at 2
		200.	.05	5.	
pink card		2.	gives baseline at T=0		
		200.	.05	5.	
		126.	1.	1.	continuation T.C.
		1.	.3		during passive recovery
		200.	.05	25.	
pink card		2.	.3		
		200	.05	25.	
		126.			restart T.C.
		1.	gives baseline at T=0		During $\mathcal{E}=10$ at 4
		200.	.05	5.	
pink		4.			
		200.	.05	5.	
		126.	1.	1.	continuation T.C.
		1.	.3		during passive recovery
		200.	.05	49.	
pink		4	.3		
		200.	.05	49.	

pink cards to be replaced for other $\mathcal{E}$ locations.
Suspect that Cpt. 2 will have wrong time spacing, because it does not have the maximum time value originally intended.

Datapoints here are 50+50+6+6+26+26+6+8 = 112+66 = 178

∴ could increase the two 25. to 49. if needed.

3/17/65 65.100 series

Thinking of setting up New Equiv. Cyl EPSP Series.

Old 730.900 Series used $\Delta t = 1$ $\lambda_{ij} = 1.25$

$\lambda_{oi} = .05$ etc.

But now use $\Delta T = .05$

$\lambda_{oi} = 1$ $\lambda_{ij} = 25$.

Also let Gt.12 be E source and set = 1.0

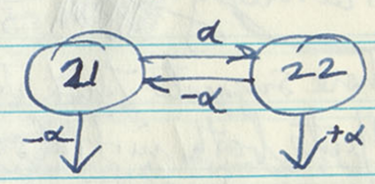
11 be J source & set = −0.1

let ordinate scale be from −0.1 to +0.35

Don't bother with dependence relations, except possibly for λ_{ij}, but plan to be explicit about each perturbation. The initial values of all λ shall be ~~s~~ set values.

Also, ~~try~~ try to set up sinusoidal input problem

Mones has pointed out that



both $\lambda_{jj} = 0$

If $\lambda_{22,21} = +\alpha$

$\lambda_{21,22} = -\alpha$

$\lambda_{0,21} = -\alpha$

$\lambda_{0,22} = +\alpha$

diff. eqn has sinusoidal soln

root is $\pm i\alpha$

i.e. get $\alpha = 2\pi f$

if f = 100 cps, $\alpha \doteq 600$ (628) for t in secs

~~But for $(\alpha\tau)\left(\frac{t}{\tau}\right)$ need $(600)(4\times10^{-3}) \approx 2.4$~~ say 2.5

Let I.C. be 100 in 21

& let 22 feed 1 i.e. have $\lambda_{0,22} = \alpha - \lambda_{1,22}$

65.101

$\varepsilon = 5$ in ② gave peak of 0.26 in ② } at $T = 0.25$
and peak of 0.23 in ① }

$\varepsilon = 10$ in ④ gave peak of 0.365 in ④ at $T = 0.25$
0.192 in ① at $T = 0.35$

The Kappas were made much too small.
Actually, these amplitudes are better regarded as summations because, for 50 mV resting pot., these corresp to 10 to 12 mV epsp

Comparing with p. 90, note that in ② $(1+\varepsilon+g)\Delta T = (6)(.25) = 1.5$

$\therefore$ Ratio predicted for isolated patch would be $\frac{1-e^{-1.5}}{1.5} = \frac{1-.223}{1.5}$
$\simeq \frac{0.777}{1.5} = 0.516$

Whereas actually from computer results $\frac{.26}{5(.11)} = \frac{.26}{.55} = 0.47$

The agreement here suggests that the μ_{ij} effect is small, presumably because it effects both initial slope and final value in a similar way, as does ψ for isolated patch. This is another example of going faster toward a lower st. st. value.

Now look at ④ where have $(11)(.25) = 2.75$ Ratio $\frac{1-e^{-2.75}}{2.75} = \frac{1-.064}{2.75}$
$\simeq \frac{.936}{2.75} = 0.34$

whereas actually from computer results $\frac{.365}{5(.2)} = 0.365$

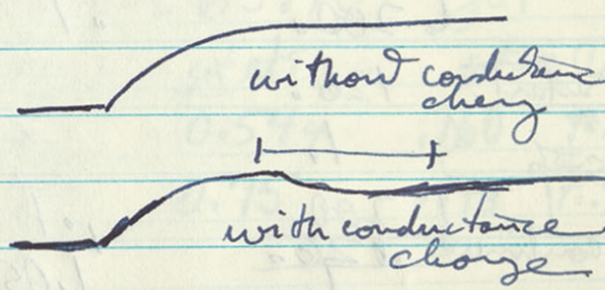
which is also very close.

3/18/65

With regard to effect of peripheral E upon soma impedance measurements, note that I can avoid the epsp itself by simply not connecting to source cpt. i.e. leave $\lambda_{i,12}$ zero & $\lambda_{o,12}$ zero and change only $\lambda_{o,i}$, thus testing only the conductance change without complication by epsp voltage, then don't need to use both + and −

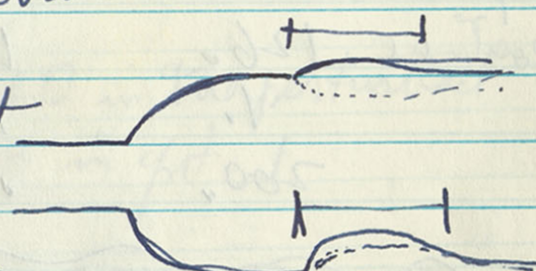
i.e. for applied current step

and perhaps



Difference would provide a measure

with epsp also present, might expect



If the shift is small, then the change in epsp would be small. Then adding two records should give twice the epsp

Subtracting should give twice that for zero source

Could do this with sigmas, esp. if make chain shorter and have two representatives.

3/19/65

65.201 13 compartments 1-12 plus ~~20~~ 13
where #~~20~~ 13 is source for const. current.

Data Cards Had to rerun with #20 renamed #13

	1.		.9	
step	1.			
	200.	.1		40.
continue	126.	1.	1.	
G on	1.	4.1		
	200.	.1		14.
restart	126.			
step	1.			
	200.	.1		10.
continue	~~126.~~	~~1.~~	1.	
	1.	1.05		
G square pulse	200.	.05		5.
continue	126.	1.	1.	
	1.	1.3		
	200.	.05		29.

Add initial condition in ~~20~~ 13, also restore at 2nd T.C.
Add $\lambda_{1,20} = 1.$ and $\lambda_{0,20} = -1.$ to original set

T.C.	26			10
	0	6	21.	11
	26			11
	0	6	1.	12
	26			12
	0	6	21.	13
	26			13
	0	6	1.	14
	26			14

3/18/65

Puzzle – missing the output listing of 6551 – 6560 (~~3~~ 2/25/65) which was set up on page 64 and checked over on p. 69. Fortunately, can manage without it because of 3/2/65 run which I do have. (This was left on my desk →) whereas other one was probably left on top of stack in the bookcase. Did someone borrow it?

3/19/65

Set up 65.102 after looking over 65.101 got
(see pp 92 & 94)

		got at ε	got in ①	
Decide to repeat for	ε = 20 in ⑥	0.544	.160	T=.5
	ε = 40 in ⑧	0.75	.143	T=.75

Use Kappa = 0.4

Reduce the decay data points to 20 in the perturbed compartments. Increase to 49 in cpt. 1

Made duplicate decks to facilitate setting up 65.201 for current step applied to soma.

For first test, put conductance change in 6 ~~without~~ but with equilibrium potential equal to resting.

cf. p. 94 — 65.102 here in ⑥ have $(1+\varepsilon+\gamma)\Delta T = (21)(.25) = 5.25$; $\frac{1-e^{-5.25}}{5.25} = \frac{1}{5.25} = .19$

Actually have $\frac{.544}{5(.345)} = .316$ but this is already down

Perturbed Compartment				Peak in 1	at T=
2	65.101	$\mathcal{E}=5$	0.26	0.23	0.25
	65.106	4.	0.2165	0.19035	
	65.104	$\mathcal{E}=2.5$	0.144	0.126	0.25
	65.106	2.	0.118	0.103	"
4	65.101	$\mathcal{E}=10$	0.365	0.192	0.35
	65.107	9.	0.3394	0.178	
	65.104	$\mathcal{E}=5$	0.2162	0.1113	0.35
	65.107	4.5	0.1981	0.1018	"
6	65.102	$\mathcal{E}=20$	0.544	0.160	0.50
	65.103	$\mathcal{E}=10$	0.360	0.1024	0.50
8	65.102	$\mathcal{E}=40$	0.75	0.143	0.75
	65.103	$\mathcal{E}=20$	0.575	0.1045	0.75

Note that Phil & Bob told me their resting potentials are around 50mV. Important to know if this low value is due to dendritic $\mathcal{E}$ background, or mild somatic injury, If mild somatic injury, need to add this to I. C., i.e. like a steady state with cathodal current.

3/22/65

Resubmit 65.201 with cpt #20 renamed #13

65.202 3/23/65 Resubmit with rescaling and call for extra time on card 3.

Put in 65.103 like 65.103 with ε values halved.
65.104 like 65.101 " " ".

Then one can conclude something about the amount of non-lin for simultaneous summations at common locations.

Also, can compare $\varepsilon = 20$ in 8 for $5\Delta T$
65.105 with $\varepsilon = 100$ in 8 ~~for~~ one ΔT
and with $\varepsilon = 20$ in 8 for one ΔT

Had to resubmit with some additional data cards.

This permits contrast between {highly focussed summation / more dispersed summation

ie. $\varepsilon = 20$ for $5\Delta T$ represents 5 of $\varepsilon = 20$ for one ΔT, in sequence
whereas $\varepsilon = 100$ for one ΔT " " " " ", simultaneous

Interesting to compare peaks,
Most interesting to see if $\varepsilon = 100$ for one ΔT can appreciably steepen rate of rise at cpt. 1.

See over page 105

3/22/65 – Phoned Tom Reese about writing up granule-initial story as a short note. He seemed interested, but wanted to talk with Brightman. He will write Gordon about his visit to Retina Foundation & I will write to Gordon about this possible note to Science. Maybe pair of notes, one from me + Gordon + one from ~~Brightman~~ Reese + Brightman.

3/23/65

① Tom Reese called back & expressed interest in joint paper.

② Dan Pollin, working with Dieter Lux, called to ask about analysis of soma-dendritic transients. They have been ~~according~~ recording IPSP, current steps & conductance changes in Betz cells. Their IPSP are as large as 8 to 10 mV

They claim 40 to 60% conductance change

Their "time constants" do not take dendrites into account. They ~~get about~~ 10 meg R_N. I sent them my Exp. Neurol reprints and the page on Sholl from NMRI report.

They may call me back.

He thinks their IPSP data is best & most suited to quantitative analysis. However, he does not yet seem to have a clear model. I said that if they are prepared to specify details for a model, we might be able to do some calcs. In particular, whether their prolonged G_i is sufficient to account for their I.PSP.

3/24/65 Setup 65.106 ~~like 65.104 but with ε = 2.~~

" ε = 2. in ②, ε = 4.5 in ④

.107 ε = 4. in ②, ε = 9. in ④

3/24/65

65.202 worked

Ten Compartments with $\mu_{ij} = \lambda_{ij} = 25.$ $\lambda_{oj} = 1.0$

Steady state values for an influx of 1.0 per τ into 1

are as follows

1	0.18855
2	0.15609
3	0.12988
4	0.10886
5	0.09219
6	0.07921
7	0.069405
8	0.062372
9	0.057835
10	0.055610

for a step on, transient in 1 value reaches 0.1836 by T = 3.0

This is $\frac{.005}{.188}$ or approx 2.5% from st. st. in 1

probably farther from st. st. in 10

Now test $\mathcal{E} = 20$ in 6 with $E_c = E_r$, in other words $\lambda_{0,6} = 21.$

Such an $\mathcal{E}$ with $E_c = E_r = 1$ for $\Delta T = 0.25$, in 6, gives an epsp peak of 0.16 in 1

However, conductance pulse change alone, applied at T = 1.0 after onset of current step (i.e. when amplitude in 1 is up to 0.15), depresses this transient only by about 3% at T = 1.36 i.e. $\frac{.1606 - .1555}{.1606} \approx \frac{.005}{.161}$

Maintained conductance change in 6 leads to st st. effect $\approx$ 18%

Note for single $\mathcal{E}=20$ in 8 for $\Delta T=.05$, $\frac{\text{peak in 1}}{\text{peak in 8}} \simeq \frac{.029}{.345} = .084$ ratio

for 5 of these simultaneous ~~sequence~~ $(\mathcal{E}=100)$ $\frac{.070}{.769} = .091$ ratio

for 5 in sequence ~~simultaneous~~ $(\Delta T=.25)$ $\frac{.1045}{.575} = .182$ ratio

i.e. 5 simultaneous increases peak in 1 + 8 by approx same factor (2.3)

but 5 in sequence ~~increases~~ does less well for peak in 8

but, ~~because of less~~ ~~than~~ in does better for peak in 1

Now look at slope at half max in 1

$\mathcal{E}=20$ in 8 for $\Delta T=.05$

half up at 0.27

peak at T = 0.65

half down at T = 1.7

slope half way up

$\frac{.0171-.0128}{.3-.25} = \frac{.0043}{.05} = .083$

$\mathcal{E}=100$ in 8 for $\Delta T=.05$

half up at 0.27

peak at 0.65

half down at 1.65+

$\frac{.0426-.0322}{.3-.25} = \frac{.0104}{.05} = .208$

ratio $\frac{208}{83} = 2.5$

approx same as ratio of peak amplitude

$\mathcal{E}=20$ in 8 for $\Delta T=.25$

half way up .35

peak at .75

half down 1.8

Slope = 0.29

ratio = $\frac{289}{83} = 3.48$

similar to peak ratio.

3/25/65

65.105 tested $\varepsilon = 20$ in ⑧ for $\Delta T = .05$
$\varepsilon = 100$ in ⑧ for $\Delta T = .05$

to be compared with previous $\varepsilon = 20$ in ⑧ for $\Delta T = .25$

	peak in ⑧	peak in ①	
$\varepsilon = 20$ in ⑧ for $\Delta T = 0.05$	~~0.02~~ .34518	0.02869	$T = .65$
$\varepsilon = 100$ in ⑧ for $\Delta T = 0.05$	.7690	0.07017	.65
(5) Ratio $\frac{\text{larger}}{\text{smaller}}$	(2.23 for peaks)	(2.44)	

presumably area ratio is 2.44

from $\varepsilon = 20$ in ⑧ for $\Delta T = 0.25$	.575	0.1045	.75
(5 spread out) Ratio	(1.67 for peaks)	(3.65)	

65.106 & 107 added to page 98 in green. provide good match for smaller of each pair

65.203 uses shunt = 40+1 in ⑧

See p, 110

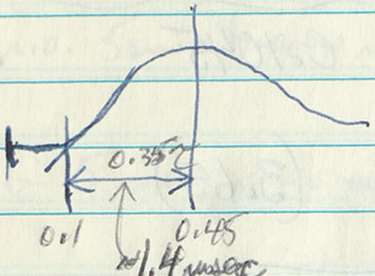
note that in ① $\varepsilon = 20$ in 8 for $5\Delta t$ gives most

and in ⑧ $\varepsilon = 100$ in 8 for $1\Delta t$ gives most

presumably too much leaks away during $5\Delta t$

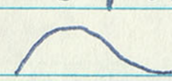
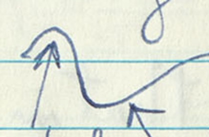
Actually, they must now reinterpret their results. What they have shown is that many of the epsp are generated in the dendrites, now that they know my results. My results show that time to peak can be obtained even from dendritic synapses. Their time to peak is from 0.4 to 1.5 msec, average about 1.1

But all of these epsp, computed for E in ②, ④, ⑥, ~~⑧~~ will fit this range. In the case of E in ⑥



This was the most telling point to Phil Nelson.
Tom had hoped to rule out the peripheral locations on this basis.

Furthermore, Tom and I figured out that several additional observations would fit the hypothesis that many epsp are compound, with the earliest part due to peripheral E and the later part due to central E. This seemed

* to fit the peculiar turn over during sustained applied depolarization  goes to 

which could reverse driving pot. at soma, while not in periphery.

Could try to simulate both of these.

* The other observation is the fact that when he does get a detectable conductance change, it occurs often after peak of epsp, which could be explained if early part due to peripherally located E.

3/25/65

K. Frank, Tom Smith, Phil Nelson & Roy Wuerker came over this morning. By means of 65.202, I convinced them that they could not detect such conductance changes. Tom thought he had proved epsp were not generated by conductance changes, but required current injection. He thought that an electric synapse would inject current without causing a measurable conductance change. I think I convinced them that this was not so; I argued that this is also formally a conductance change, i.e. that synaptic plaque low conductance would be opened to extracellular pot. by the knob stem conductance change. They seemed to think more of the presynaptic spike voltage, forcing current through a sizable synaptic resistance, and Tom had convinced himself that there would be no measurable conductance change involved with such current injection, even at the soma. Some of the flaws of his argument probably result from using steady state considerations.

* Forgot to ask them the amplitude of their sinusoidal testing voltage, this could make a little difference, but probably not much

Since histology has shown no difference, so far, for E or I synapses, could suggest that electric hypoth would work for both.

With regard to their phase sensitive detection, they do not feel confident of detecting a conductance change of less than 10%

G/Gr = 4 in (2) aimed at $\mathcal{E}$ = 3 in (2) which is guessed expected to give peak epsp ≈ 0.14 seep. 98

also G/Gr = 7.5 in (4) aimed at $\mathcal{E}$ = 6.5 in (4) which is guessed to give peak epsp ≈ 0.14

Could also redo series for $\mathcal{E}$ = 20 in (8)
10 in (6)
These are aimed at 4.5 in (4)
epsp peak ≈ 0.102 2.0 in (2)
in (1)
seep. 98

G/Gr	
21	65.206
11	65.207
5.5	65.208
3.0	65.209

3/29/65 Set up to monitor perturbed epsp

65.206 purposely made base λ_{08} = 21. so that can get st. st. from epsp. size. This required explicit zero T.C.

also 65.207 λ_{06} = 11.

.208 λ_{04} = 5.5

.209 λ_{02} = 3.0

3/25/65

Setup 65.204 with $G/G_r = 7.5$ in (4)
65.205 $G/G_r = 4$ in (2)

got back 3/26/65

Consider setting up 65.301 with sinusoid produced by 13 & 14
i.e. increase opt number to 14
Then, looking at p. 93, set ~~8~~ look at 1. & 6.

also, must place zero in mid paper, i.e. set 1. −11.25
1. +11.25

already have $\lambda_{1,13} = 1.$ as in 65.200 series
set $\lambda_{13}, \lambda_{14} = +2.5$
$\lambda_{14}, \lambda_{13} = -2.5$
$\lambda_{0,13} = +2.5 - 1$ so that $\lambda_{13,13} = 1. \cancel{+}\, 2.5 + 1.5$
$= +1.5$
$\lambda_{0,14} = -2.5$

Set I.C. in 13 be 1. as in 65.200 series
14 0.

200	.1	40. for 1. & 6.
126.		
1.	40.05	
200	.05	4.
126. same for 6.		
1.	4.3	
200.	.05	24.

i.e. Two time changes only.

If sinusoidal works, try two chains of 5 with $\mu_{ij} = 6.25$
and run 180° out of phase and use summer. Use one as control for other.

Got body 3/26/65 65.204 65.205 see previous page

These were aimed at epsp = .14

	65.204	65.205	65.202	65.203
G/Gr	4	7.5	21	41
in comp.	2	4	6	8
st. st. control	.1885	.1885	.1885	.1885
≈ st. st. shunted	≈ .1400	.1480	.1541	.1660
difference	.0485	.0365	.0344	.0225
% reduction	25.7%	19.3%	18.3%	≈ 12%
Brief G/Gr	1.25	T = 1.30		1.30
control value at ~~1.25~~	0.1590	0.1607	.1607	.1607
dipped value at 1.25	0.1409	0.1506	.1555	.1592
difference	.0181	0.0101	.0052	.0015
% dip	11.4%	6.3%	3.2%	0.9%

epsp peak from p .98 ~~0.14~~

3/26/65 – 3/29/65

Refer back to p. 81 & earlier. Time to return to kinetic model windup. Question of figs. like those sketches on pp 66 and 73.
See esp. p. 71

Based upon 6556 & 6566

Now try the following

R_1	R_2	R_3	R_4	R_5	R_6	R_7	
.1+4	.1	.25+2	.1-4	.1+2	.1-5	.1+2	6581
"	"	."	"	"	"	.5+1	6582
"	"	.15+2	-	-	-	-	6583
-	-	-	-	.15+2	-	-	6584
.2+4	-	-	-	-			6585
				.10+2	-	-	6586
				.05+2	-	-	6587

2345	12	27	
126.	1.	1.	for continuation

Setup 65.208 with $\lambda_{04} = 5.5$

65.209 with $\lambda_{02} = 3.$

65.302 with 126. card fixed but not actual perturbation. This is to be a control. Could add also cft. 13 with kappa = 0.1

Refer to p. 98

Those all give epsp ≈ 0.103, when $E_E - E_R = 1$

	65.209	65.208	65.207	65.206
G/G_2	3.0	5.5	11	21
Comp.	2	4	6	8
st-st. control	.1885	.1885	.1885	.1885
st-st shunted.	.1518	.1555	.1614	.1687
difference	.0367	.0330	.0271	.0198
% reduction	19.5%	17.5%	14.4%	10.5%

	1.25	1.30			
Control 1.30	.1590	.1607	.1607	.1607	.1607
dropped 1.30	.1465	.1490	.1533	.1575	.1596
difference	.0125	.0117	.0064	.0032	.0011
	7.8%	7.3%	3.98% 4%	1.99% 2%	0.68%

3/30/65

WXR 752C — 6581 — 6587 ran successfully (p. 111)
also 65.206 & 65.207 ran successfully (Seen also in perturbed compartment) wrong 126. card
and 65.301 Sinusoidal worked up to time change.
∴ Quite a lot to digest, before setting up next runs.

65.301 — Sinusoidal period came out 2.5 τ as intended. However, starting cpt. 13 with I.C. = 1. may not be quickest way to steady state sinusoidal. Might be better to start with 13 at zero and 14 at −1.

Also, may wish to monitor compartment 13, although not really necessary. would need $Kappa_{13} = 0.1$

This test shows that cpt. 6 follows pretty well, even after one cycle. It lags approx by 0.4 τ

In 1		In 6	
1st. peak ≈ 0.813	at T ≈ 0.4	.0207	T = 0.7
0	at T ≈ 0.88	0	~ 1.25
−.1084	1.50	−.0291	1.90
0	~ 2.18	0	~ 2.58
+.1045	2.80	+.0265	3.20
0	~ 3.40	0	~ 3.80
−.1050	4.0		

65.302 output to compare with 65.301

Problem with scaling and Kappas

Did succeed in shifting phase, ~~but not quite as intended.~~ ? 180° away ?

Did st. st. seem to arrive sooner in 1 ?

1		6	
peak −.1206	at T=0.90	peak −.3657	T=.120
zero	1.56	zero	2.0
peak +.1010	2.20	+.2442	2.60
zero	2.80	zero	3.17
peak −.1065	3.40	−.2788	3.80
zero	~ 4.05	zero	4.45
peak +.1049	4.65	+.2687	5.05
zero	5.30		

6 rel to 1

lag = 0.4τ

as before

in 65.301

see previous page

~~Similar, but not really better~~

for 13

−.9975	at T=.60
zero	1.25
+.9993	1.90
zero	2.50
−.9946	3.10
zero	3.85
+.99988	4.40
zero	5.025

4/2/65 Was out 2 1/2 days on sick leave
Received Airmail Special from Gordon Shepherd, and telephone call from Tom Reese regarding the proposed joint paper. - see p. 86
reply to letter of March 23

4/5/~~4~~ 4/6/65 roughed memo to ~~Gordon~~ Gordon Shepherd, Tom Reese & Milton Brightman

Complete table on p. 112 based on output received 3/31/65
65.208 & 65.209

look at 65.302, opposite page.
There was a goof on the amplitude scaling.
However, did get perfect sinusoidal in 13
which drives 1
& can get phase lag 13 → 1 → 6
13 → 6

2nd pos peak in 13 was at T = 4.40
1 4.65
6 5.05

$\frac{\pi}{5}$ ∴ 1 lags 13 by 0.25τ $\theta = \left(\frac{25}{250}\right)(360) = 36°$

$\sim\frac{\pi}{3}$ 6 lags 1 by 0.4τ $\theta = \left(\frac{40}{250}\right)(360) = 57.8°$

$\sim\frac{\pi}{2}$ 6 lags 13 by 0.65τ $\theta = \left(\frac{65}{250}\right)(360) = 93.5°$

Could get all of this by rerunning but plotting only last half cycle

4/8/65

Today several separate lines of thought converged upon the subject of field effects.

① Bullock asked me about them in March with regard to his electric fish & also others re ②

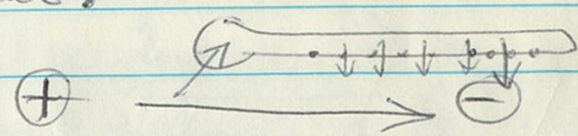
② Foy & O'Brien pp 888-890 in Feb. 19, 1965 issue of Science

③ Cochner, presumably a graduate student at Case Inst. of Tech, asked me about my B.V.P calc. on p. 164 of Biophys J. paper.

④ It occurred to me this morning that the field generated by the granule cells might itself provide the inhibition of the mitral cells.

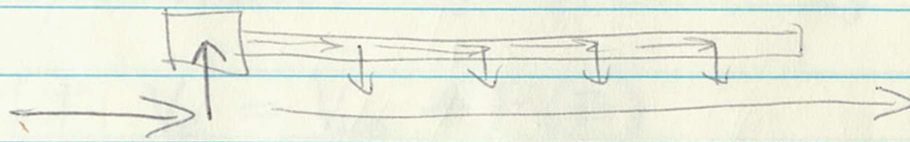
Having pondered all this, I begin to think it all fits ~~together~~ together. The gradient generated by the granule cells is in the correct direction, & also of significant magnitude, to provide anodal stimulation of the mitral somata (the steepest gradient is in the right place). If dendrodendritic synapses should also provide a lower ~~conducta~~ resistance path, this could provide for more invasion of the anodal current, esp. if this higher dendritic membrane conductance does not depolarize, the conditions would be ideal.

Because of extended dendritic conductance change, it would be even more important to have wax gradient at MBL



Question is, how much current would flow across soma membrane to cause hyperpol. & also, how much stabilization provided, apart from hyperpol.

In this case, BVP is extracell gradient given
extensive dendritic J but perhaps with $E_j = E_r$
Effect would be to reduce impedance for current thru cell.
Could do a simulation of this problem, similar to simulation done for Smith & Frank, with L/λ smaller.



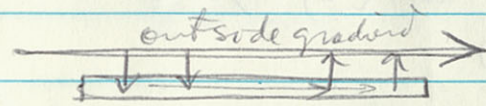
one way to think of it is to say that dendritic J reduces λ
and this reduces $G_D \propto \lambda r_i \propto \sqrt{r_m r_i}$

it really depends approx upon st. st. G_S/G_D
because will det how ~~pot~~ externally applied pot., ideally applied ext. to versus ext. to all dendrites, would divide across soma membrane, ~~versus~~ across dendritic system. If $G_S/G_D \leq 1/5$ to $1/10$, get anodal hyperpol across soma membrane to be $5/6$ or $10/11$ of total applied. — But this simple approach neglects the dist of applied pot. along dendritic length. For this, must recheck original B.V. method.
See p. 121

But now, consider Fox & O'Brien. My explanation will fit their data if I am correct in assuming that their evoked pot. recordings are surface versus microelectrode (or focal pos. downwards) as would seem to be the case from Chang's statement in Handbook that ~~princip~~ primary response is surface pos. If this is the case, then F+O data shows that surface +, deep −, agrees with enhanced firing.

4/9/65

From old folder of notes for Biophys ~~Congress~~ Calculations.
First batch 5/18/61, 6/5/61, 6/7/61, 7/7/61
↑ numerical calcs.



Express rel to Z of equivalent cylinder.

Let $V_e = V_{eo} + F(Z)$ where $V_{eo} = V_e(0)$
Where F(Z) contains the resultant applied $F(0)=0$
non-uniformity. It is a forcing function.

For equivalent cylinder $\frac{\partial^2 V_i}{\partial Z^2} = I_m R_m$ N.Y. Acad p 1080 eq. 22 with $K=0$

and ~~$I_m R_m$~~
for passive membrane $I_m = \frac{V_i - V_e - E_r}{R_m}$

(although, more generally, have eq. 1 of N.Y. Acad. paper)
or eq (2) $I_m R_m = \tau \frac{\partial V}{\partial t} + k^2 (V - V^*)$

For steady state, $\therefore \frac{\partial^2 V}{\partial Z^2} = k^2 (V - V^*)$ see eq. 30 of that paper
But this is not what we want here

Now, $V = V_m - E_r = V_i - V_e - E_r = V_i - (V_{eo} + F) - E_r$
Define $U = V_i - V_{eo} - E_r = V + F(z)$

Note that $\frac{\partial^2 V_i}{\partial Z^2} = \frac{\partial^2 U}{\partial Z^2} \neq \frac{\partial^2 V}{\partial Z}$ in general for F(z) not a constant

Thus, the trick is to solve for U, with F(Z) as forcing fcn
See over.

For purposes of verifying particular soln

Note, differentiating a convolution is a special case of the following;

if $$\Psi(Z) = \int_{g(Z)}^{f(Z)} \Phi(\tau, Z)\, d\tau$$

Then $$\frac{d\Psi}{dZ} = \Phi(f(Z), Z) f'(Z) - \Phi(g(Z), Z) g'(Z) + \int_{g(Z)}^{f(Z)} \frac{d\Phi}{dZ}\, d\tau$$

$\therefore$ ~~If~~ $$Y = F(Z) * \sinh Z = \int_0^Z F(\tau) \sinh(Z-\tau)\, d\tau$$

$$\frac{dY}{dZ} = F(Z) \sinh(0) + \int_0^Z F(\tau) \cosh(Z-\tau)\, d\tau$$

$$= 0 + F * \cosh Z$$

and $$\frac{d^2Y}{dZ^2} = F(Z) \cosh(0) + \int_0^Z F(\tau) \sinh(Z-\tau)\, d\tau$$

$$= F(Z) + F * \sinh Z$$

$$\therefore \frac{d^2Y}{dZ^2} - Y = F(Z)$$

whereas $$\frac{d^2(-Y)}{dZ^2} - (-Y) = -F(Z)$$

$\therefore$ $-F * \sinh Z$ is a particular solution

Above implies that $\frac{d}{dZ}(F * \sinh kZ) = F * k \cosh Z$

also $\frac{d}{dZ}(F * \cosh \cancel{kZ}) = kF * \sinh Z + F$

4/9/65 for passive membrane & steady state

$$\frac{d^2 V_i}{dZ^2} = V_i - V_e - E_r \quad \text{becomes} \quad \frac{d^2 U}{dZ^2} = U - F(Z)$$

B.C. $\frac{dV_i}{dZ} = 0$ at $Z=0$, $Z = Z_{max}$ becomes $\frac{dU}{dZ} = 0$ at $Z=0$, $Z = Z_{max}$

This depends only upon E_r const, because V_{eo} already const.

My 1961 procedure was to use Laplace transforms, but classical procedure should also work.

Homogeneous problem is $\frac{d^2U}{dZ^2} - U = 0$

giving general solution $U = c_1 e^{-Z} + c_2 e^{+Z}$

or $U = b_1 \cosh Z + b_2 \sinh Z$

Now, to get particular soln. → $-F^* \sinh Z$

* Talked with José & he thinks my original way of getting this solution is probably simplest & best

Namely, Laplace transform of DE gives

$$s^2 u - sU_0 - \frac{dU}{dZ}\Big|_0 - u = -f(s)$$

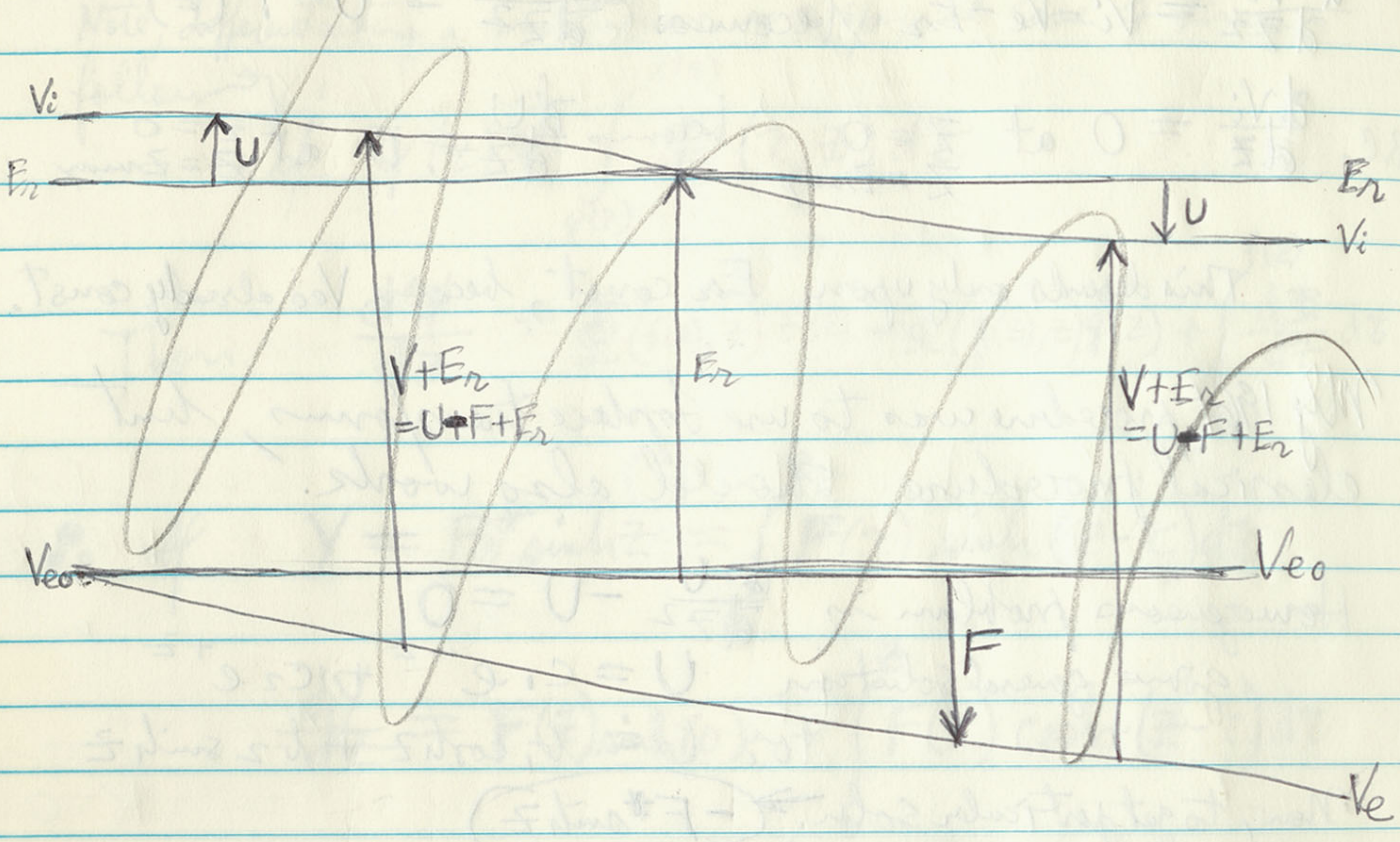
And because of $\frac{dU}{dZ} = 0$ at $Z=0$ B.C. can save several steps by putting this fact in already

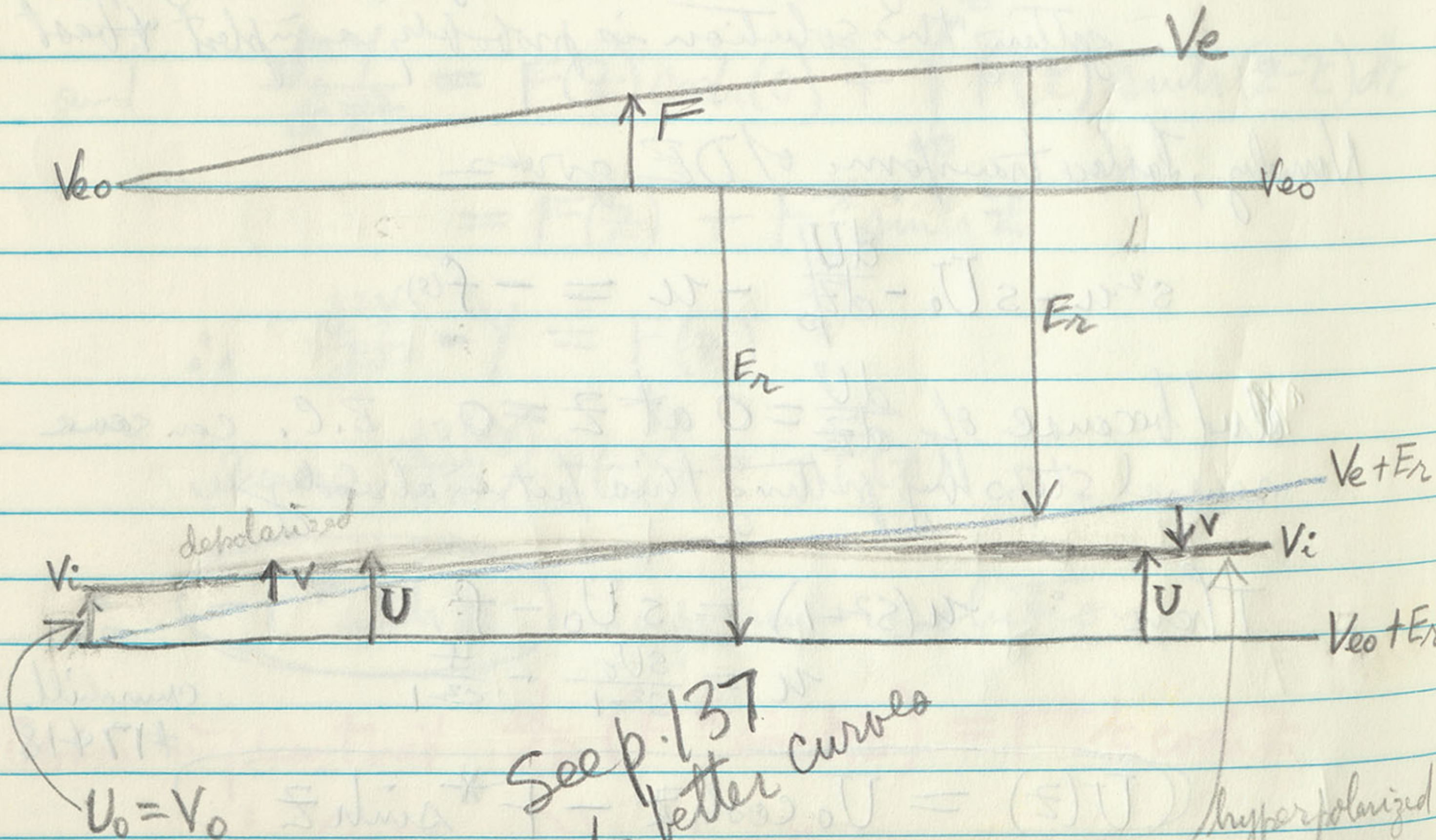
Then $u(s^2-1) = sU_0 - f$

$$u = \frac{sU_0}{s^2-1} - \frac{f}{s^2-1}$$ Churchill #17 & 18

$$U(Z) = U_0 \cosh Z - F^* \sinh Z$$

where U_0 must be determined to satisfy B.C. at $Z = Z_m$





See p. 137 for better curves

4/9/65

$$\frac{dU}{dZ} = U_0 \sinh Z - F^* \cosh Z \quad -①$$

$\therefore \frac{dU}{dZ} = 0$ at $Z = Z_m$ gives $\boxed{U_0 = \left(\frac{1}{\sinh Z_m}\right)\left[F^* \cosh Z\right]_{Z=Z_m}}$

$\therefore$ Unique soln is $\boxed{U(Z) = U_0 \cosh Z - F^* \sinh Z}$

with U_0 defined as above.

Note also, $V_0 = U_0$ and $V(Z) = V_0 \cosh Z - F^* \sinh Z - F$

To obtain $F^* \cosh Z$, note that $L_1\{F^* \cosh Z\} = \frac{s f}{s^2 - 1}$

Showed 6/5/61 as well as 5/18/61 that

for $F(Z) = kZ$, $F^* \cosh Z = k \cosh Z - k$

$$U_0 = k\left(\frac{\cosh Z_m - 1}{\sinh Z_m}\right) = k \tanh\left(\frac{Z_m}{2}\right)$$

Also, because $F^* \sinh Z = k \sinh Z - kZ$

we get $\boxed{U = k \tanh\left(\frac{Z_m}{2}\right) \cosh Z + kZ - k \sinh Z}$

also, at $Z = Z_m$

$$V_{Z_m} = U - kZ = k\left(\frac{(\cosh Z_m - 1)\cosh Z_m}{\sinh Z_m} - \frac{\sinh^2 Z_m}{\sinh Z_m}\right)$$

$$= k\left(\frac{1 - \cosh Z_m}{\sinh Z_m}\right) \quad \text{because } \cosh^2 - \sinh^2 = 1$$

$$= -U_0$$ which physical intuition demands

Consider $F = bZ$ then $F^* \cosh kZ$

$$b\int_0^Z (Z-\tau)\cosh k\tau \, d\tau$$

$$= \frac{b}{k}\int_0^Z \underset{u}{(Z-\tau)}\, \underset{dv}{k\cosh k\tau\, d\tau}$$

integrate by parts $\int u\,dv = uv - \int v\,du$

$$= \frac{b}{k}\Big[(Z-\tau)\sinh k\tau\Big]_0^Z - \frac{b}{k}\int_0^Z (-1)\sinh k\tau\, d\tau$$

$$= 0 + \frac{b}{k^2}\Big[\cosh k\tau\Big]_0^Z$$

$$= \frac{b}{k^2}\left\{\cosh kZ - 1\right\}$$

Laplace Transform

$$\left(\frac{b}{s^2}\right)\left(\frac{s}{s^2-k^2}\right)$$

$$= \frac{b}{s(s^2-k^2)}$$

$$= \frac{bs/k^2}{s^2-k^2} - \frac{b/k^2}{s}$$

inverts to

$$\frac{b}{k^2}\left(\cosh kZ - 1\right)$$

Also, consider $F^* \sinh kZ$ for $F = bZ$

$$\frac{b}{k}\int_0^Z (Z-\tau)k\sinh k\tau\, d\tau$$

$$= \frac{b}{k}\Big[(Z-\tau)\cosh k\tau\Big]_0^Z - \frac{b}{k}\int_0^Z (-1)\cosh k\tau\, d\tau$$

$$= -\frac{bZ}{k} + \frac{b}{k^2}\Big[\sinh k\tau\Big]_0^Z$$

$$= \frac{b}{k^2}\left\{\sinh kZ - kZ\right\}$$

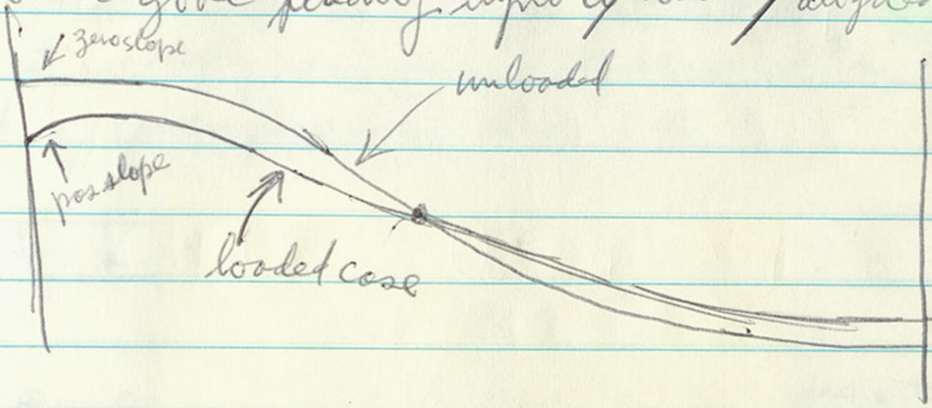
$$\left(\frac{b}{s^2}\right)\left(\frac{k}{s^2-k^2}\right)$$

$$= \frac{bk/k^2}{s^2-k^2} - \frac{bk/k^2}{s^2}$$

$$= \frac{b}{k^2}\left\{\sinh kZ - kZ\right\}$$

4/9/65

The 5/18/61 notes also included $\frac{dV_i}{dZ} = \gamma V_0 = \gamma U_0$ for the case of loading at right angles, where γ would give loading input conduct / aligned input conductance



But did not consider using $k^2(V-V^*)$ which would provide way of getting effect when there is uniform E_r everywhere.

Trick would be to redefine $W = V_i - V_{eo} - V^* - E_r$

replace U with W
$W = U - V^*$

$$I_m R_m = k^2(V - V^*)$$
$$= k^2(V_i - V_e - E_r - V^*) \qquad V_e = V_{eo} + F(Z)$$
$$= k^2 W - k^2 F$$

∴ DE becomes $\frac{d^2W}{dZ^2} = k^2 W - k^2 F$ see page 131

Can incorporate k^2 in Z to get $\frac{d^2W}{d(kZ)^2} = W - F$

Then $Z_{max} \longrightarrow k Z_{max}$

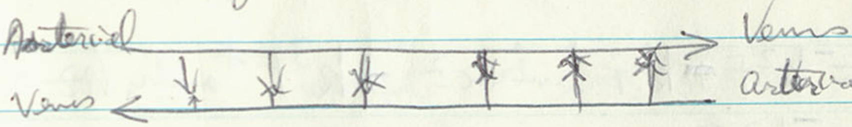
However, desirable to keep k explicit, because Z & $F(Z)$ depend~~s~~ upon geometry & resting membrane properties.

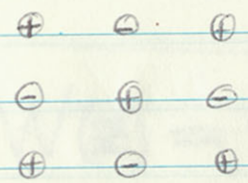
See p. 130 & 131, 133

Here have two ⊕ for every one ⊖
can solve similarly.

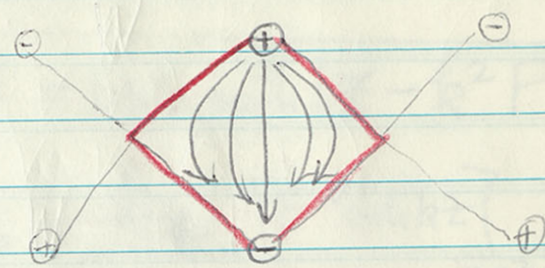
4/13/65

Spent most of day talking with Jose about the consequences of symmetry in the arrangement of countercurrent capillaries. I thought first in terms of sources & sinks, but finally we noted that we really have pair of sources with dist. sink caused by consumption in volume.





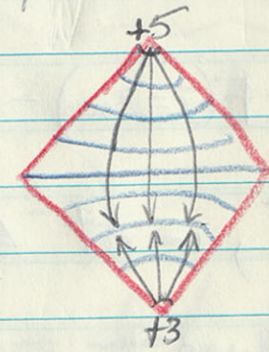
infinite lattice where ⊕ means arterial end and
⊖ means venous end.



Symmetry guarantees that red lines have zero normal gradient.

This square contains the entire problem for these two dimensions.

Also because of dist. sink, will have ~~[illegible]~~ an equipotential contour somewhere inside which also has normal gradient zero. This is the minimum value



If use orthogonal (conformal) mapping of this, can reduce diffusion in these two dimensions to diffusion in one dimension, because the gradient is zero along the equipotential contours.

To prove $-kF^* \sinh kZ$ is a particular soln for W, subst.

$$y = -kF^* \sinh kZ$$
$$\frac{dy}{dZ} = -k^2 F^* \cosh kZ$$
$$\frac{d^2y}{dZ^2} = -k^2 F + k^3 F^* \sinh kZ$$

$$\frac{d^2y}{dZ^2} - k^2 y = -k^2 F \cancel{+ k^3 F^* \sinh kZ} + k^3 F^* \sinh kZ$$
$$= -k^2 F \qquad \text{QED}$$

In other words $F(Z = Z_m) - F(0) = b Z_m$

If $Z_m = 0.5$, we get $\Delta F = b/2$ applied across $\frac{1}{2}\lambda$ cylinder

Now, if $k^2 = 4$, $k = 2$, we get $\Delta F = b/2$ applied across effectively 1λ

But the gradient of F per effective λ is now halved

And apparently what really matters is $\begin{cases} \text{(a) gradient of F per effective } \lambda \\ \text{(b) effective length.} \end{cases}$

However, this is partly artefact of const gradient with Z

4/14/65 from p. 127 Avoid changing variable Z

Thus $\frac{d^2W}{dZ^2} = k^2 W - k^2 F$

with $\frac{dW}{dZ} = 0$ at $Z = 0$ and $Z = Z_m$

Laplace transform to get $s^2 w - sW_0 - 0 = k^2 w - k^2 f$

hence $w(s^2 - k^2) = sW_0 - k^2 f$

$$w = \frac{sW_0 - k^2 f}{s^2 - k^2}$$

$$\therefore \boxed{W(Z) = W_0 \cosh kZ - kF^* \sinh kZ}$$

to obtain W_0, differentiate $\frac{dW}{dZ} = kW_0 \sinh k\cancel{Z} - k^2 F^* \cosh kZ$

see p. 122

for $\frac{dW}{dZ} = 0$ at $Z = Z_m$, get $W_0 = \frac{k}{\sinh kZ_m}\left[F^* \cosh kZ\right]_{Z=Z_m}$

Now, consider $F = bZ$, then from p. 126, get

$$W_0 = \left(\frac{k}{\sinh kZ_m}\right)\left(\frac{b}{k^2}\right)\left(\cosh kZ_m - 1\right)$$

$$= \frac{b}{k}\left(\frac{\cosh kZ_m - 1}{\sinh kZ_m}\right) = \frac{b}{k} \tanh\left(\frac{kZ_m}{2}\right)$$

This can be understood intuitively that argument of tanh is multiplied by k because of effectively greater electrotonic length but that W_0 is divided by k, because $F = bZ$ per unit effective λ, has been decreased, i.e. $\frac{dF}{dZ} = b$

but $\frac{dF}{d(kZ)} = \frac{b}{k}$

$kZ \propto \frac{x}{\lambda/k}$

using $\frac{dF}{dZ}$

Note following, where we consider possibility that $F(0) \neq 0$

Then $$F^* \cosh Z \equiv \int_0^Z F(\tau)\cosh(Z-\tau)\,d\tau$$

by parts $$= -\Big[F(\tau)\sinh(Z-\tau)\Big]_0^Z + \int_0^Z \frac{dF}{d\tau}\sinh(Z-\tau)\,d\tau$$

$$= +(\sinh Z)\,F(0) + \frac{dF}{dZ}^* \sinh Z$$

but our definitions of U & V require $F(0)=0$

$$F^* \sinh Z \equiv \int_0^Z F(\tau)\sinh(Z-\tau)\,d\tau$$

by parts $$= -\Big[F(\tau)\cosh(Z-\tau)\Big]_0^Z + \int_0^Z \frac{dF}{d\tau}\cosh(Z-\tau)\,d\tau$$

$$= -F(Z) + (\cosh Z)\,F(0) + \frac{dF}{dZ}^* \cosh Z$$

$$= \frac{dF}{dZ}^* \cosh Z - F(Z) \quad \text{even when } F(0)=0$$

Also $F^* \cosh kZ = \frac{1}{k}\frac{dF}{dZ}^* \sinh kZ$ for $F(0)=0$

and $F^* \sinh kZ = \frac{1}{k}\left\{\frac{dF}{dZ}^* \cosh kZ - F(Z)\right\}$

$\therefore$ particular soln for W can be expressed $-\frac{dF}{dZ}^* \cosh kZ + F(Z)$

4/14/65

What p. 131 has revealed is that $k^2 = 1 + \varepsilon + j$ everywhere uniform will not make $W_0 > U_0$

Intuitively, ~~this would~~ increase in U_0 better achieved by increasing conductance at anodal end. see later.

However, we must note, here that $W_0 = V_0 - V^*$

see p. 127 & N.½ Acad

$$\therefore V_0 = W_0 + V^*$$

and $V^* = \dfrac{G_\epsilon(E_\epsilon - E_r) + G_j(E_j - E_r)}{G_r + G_\epsilon + G_j}$

$$= (E_\epsilon - E_r)\left\{\frac{\varepsilon + \beta j}{1 + \varepsilon + j}\right\}$$

For the special case of $\varepsilon = 0$ and $\beta = 0$, get $V^* = \dfrac{E_\epsilon - E_r}{k^2}$ $= \dfrac{E_\epsilon - E_r}{1 + \varepsilon + j}$

For the special case, $j = 0$, $\varepsilon \neq 0$, get $V^* = \left(\dfrac{\varepsilon}{1+\varepsilon}\right)(E_\epsilon - E_r)$

Some of the apparent paradoxes for different λ can perhaps be most easily resolved by noting that

$\dfrac{dF}{dZ} = \nabla F \cdot \vec{Z}$ where $\vec{Z}$ is unit vector along axis of cylinders

$$\frac{dF}{dZ} = \frac{dF}{dx}\frac{dx}{dZ} = \lambda \frac{dF}{dx}$$ for cylindrical element.

Then $F^* \cosh Z$ can be rewritten $\dfrac{dF}{dZ}^* \sinh Z$ because $F(0) = 0$

$$= \lambda \frac{dF}{dx}^* \sinh(x/\lambda)$$

see p. 137

for the particular case where $\dfrac{dF}{dZ} = b$, get $b\displaystyle\int_0^{Z_m} \sinh Z\, dZ = b\left[\cosh Z\right]_0^{Z_m} = b(\cosh Z_m - 1)$

or if $\dfrac{dF}{dx} = c$, then get $c\displaystyle\int_0^{X_m} \sinh\left(\frac{x}{\lambda}\right) dx = \lambda c\left[\cosh\frac{x}{\lambda}\right]_0^{X_m} = \lambda c\left(\cosh\frac{X_m}{\lambda} - 1\right)$

Similarly $F^* \sinh Z = \dfrac{dF}{dZ}^* \cosh Z - F(Z) = \lambda \dfrac{dF}{dx}^* \cosh\left(\frac{x}{\lambda}\right) - F(Z)$ see left

$$V = V_0 \cosh\frac{x}{\lambda} - \lambda C \sinh\frac{x}{\lambda} \qquad \text{for } \frac{dF}{dx} = C$$

$$U = V + F = V_0 \cosh\frac{x}{\lambda} - \lambda C \sinh\frac{x}{\lambda} + Cx$$

also, see p. 137, thus

$$V = \lambda C \tanh\left(\frac{x_m}{2\lambda}\right)\cosh\frac{x}{\lambda} - \lambda C \sinh\frac{x}{\lambda}$$

Thus, for $\lambda_1 = 1$ mm of p. 137

got $V = \tanh(0.5)\cosh\frac{x}{\lambda} - \sinh\frac{x}{\lambda}$ mV

$= 0.4621 \cosh\frac{x}{\lambda} - \sinh\frac{x}{\lambda}$

for $\lambda_2 = 0.2$ mm

$$V = 0.1973 \cosh(5x) - 0.2\sinh(5x) \quad \text{mV}$$

4/14/65 Recap pp 121–134

Particular solution for $U = V + F$ can be expressed $-F^* \sinh Z$

or $\boxed{F - \frac{dF}{dZ}^* \cosh Z}$

which shows that particular soln for $V = U - F$ can be expressed simply

$-\frac{dF}{dZ}^* \cosh Z$

Also, the complete solution can now be expressed

$$\boxed{V = V_0 \cosh Z - \left(\frac{dF}{dZ}\right)^* \cosh Z}$$

where $V_0 = U_0 = \frac{1}{\sinh Z_m}\left[F^* \cosh Z\right]_{Z=Z_m}$

$= \frac{1}{\sinh Z_m}\left[\frac{dF}{dZ}^* \sinh Z\right]_{Z=Z_m}$

But, of course, $V_i = \underbrace{V_{(Z)} + F_{(Z)}}_{U(Z)} + \underbrace{V_{eo} + E_r}_{\text{constants indep't of } Z}$

also, note that $\frac{dU}{dZ} = U_0 \sinh Z - \frac{dF}{dZ}^* \sinh Z$

whereas $\frac{dV}{dZ} = U_0 \sinh Z - \frac{dF}{dZ} - \frac{dF}{dZ}^* \sinh Z$

Thus, at $Z = 0$, $\frac{dU}{dZ} = 0$, and $\frac{dV}{dZ} = -\frac{dF}{dZ}$

at $Z = Z_m$, $\frac{dU}{dZ} = 0$, and $\frac{dV}{dZ} = -\frac{dF}{dZ}$

---

also for p. 131 + 132 get $W(Z) = W_0 \cosh kZ + F(Z) - \frac{dF}{dZ}^* \cosh kZ$

and $V = W + V^* - F$

$= W_0 \cosh kZ + V^* - \frac{dF}{dZ}^* \cosh kZ$

$\lambda = 1\,mm$ for $C = 1\,mV/mm$

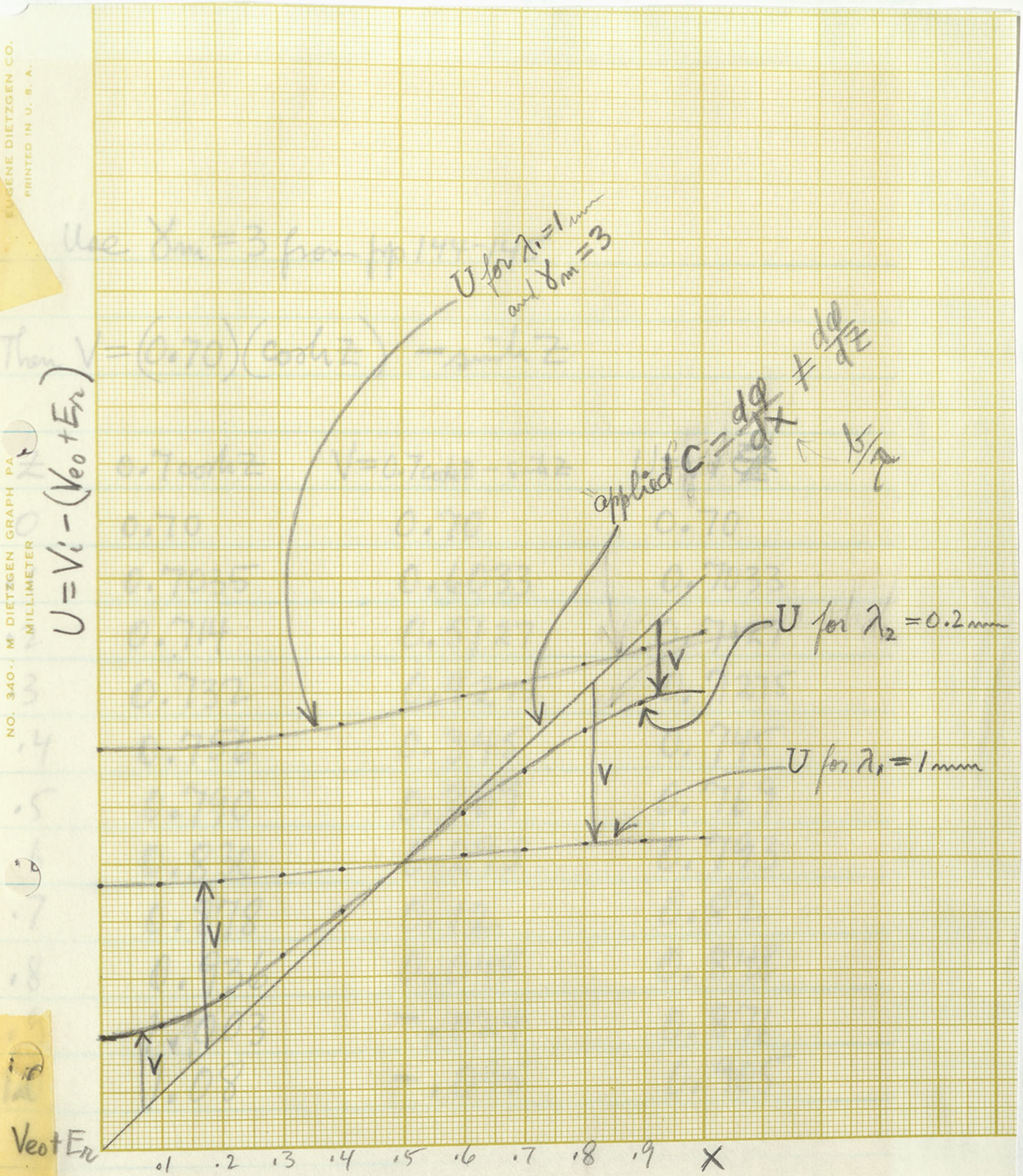
X_{mm}	$\sinh\frac{x}{\lambda}$	$\cosh\frac{x}{\lambda}$	$0.4621\cosh\frac{x}{\lambda}$	V in mV	$U = V + CX$
0	0	1.0	0.462	0.462	.462
.1	.1002	1.0005	0.464	.364	.464
.2	.2013	1.020	0.471	.271	.471
.3	.3045	1.045	0.483	.178	.478
.4	.4108	1.081	0.499	.088	.488
.5	.5211	1.128	.521	0	.50
.6	.6367	1.185	.548	−.089	.511
.7	.7586	1.255	.579	−.180	.520
.8	.8881	1.337	.617	−.271	.529
.9	1.027	1.433	.662	−.365	.535
1.0	1.175	1.543	.713	−.462	.538

Symmetric except for slide rule error

$\lambda = 0.2\,mm$

X	x/λ	$\sinh\frac{x}{\lambda}$	$\cosh\frac{x}{\lambda}$	.1973 cosh	.2 sinh	V	U
0	0	0	1.0	.1973	0	.1973	.1973
.1	.5	.5211	1.128	.223	.104	.119	.219
.2	1.0	1.175	1.543	.304	.235	.069	.269
.3	1.5	2.129	2.352	.464	.426	.038	.338
.4	2.0	3.627	3.762	.742	.725	.017	.417
.5	2.5	6.050	6.132	1.21	1.21	0	.50
.6	3.0	10.02	10.07	1.986	2.004	~.02	~.58
.7	3.5	16.54	16.57			~.04	~.66
.8	4.0	27.29	27.31			~.07	~.73
.9	4.5	45.00	45.01			~.12	~.78
1.0	5.0	74.20	74.21			~.20	~.80

6/14/65



$U = V_i - (V_{eo} + E_r)$
U for $\lambda_1 = 1$ mm and $\gamma_m = 3$
applied $C = \frac{dq}{dx} \neq \frac{dq}{dt}$
b/τ
U for $\lambda_2 = 0.2$ mm
U for $\lambda_1 = 1$ mm
V
V
V
V
$V_{eo} + E_r$
.1 .2 .3 .4 .5 .6 .7 .8 .9 X

6/14/65

Use $\gamma_m = 3$ from pp 144-145

Then $V = (0.70)(\cosh Z) - \sinh Z$

Z	$0.7 \cosh Z$	$V = 0.7\cosh Z - \sinh Z$	$U = V + Z$
0	0.70	0.70	0.70
.1	0.7035	0.6033	0.7033
.2	0.714	0.5127	0.7127
.3	0.732	0.4275	0.7275
.4	0.756	0.345	0.745
.5	0.790	0.269	0.769
.6	0.830	0.293	0.793
.7	0.878	0.12	0.82
.8	0.936	0.048	0.848
.9	1.003	-.024	0.876
1.0	1.08	-.095	0.905

4/14/65

Now compare two cylinders placed in the same $\frac{dF}{dx}$
of same length
but of different λ, λ_1 and λ_2

Let $\frac{dF}{dx} = C$, then $\frac{dF}{dZ} = \lambda C$

$0 \le X \le X_m$, then $Z_m = X_m/\lambda$

$$\therefore V_0 = U_0 = \left(\frac{1}{\sinh \frac{X_m}{\lambda}}\right)\Big[\overset{\frac{dF}{dZ}}{\lambda C} * \sinh \cancel{Z}\Big]_{Z=Z_m} \quad \text{or} \quad \Big[\overset{\frac{dF}{dx}}{C} * \sinh \frac{X}{\lambda}\Big]_{X=X_m}$$

$$= \left(\frac{1}{\sinh \frac{X_m}{\lambda}}\right)(\lambda C)\left(\cosh \frac{X_m}{\lambda} - 1\right) \qquad (\lambda C)\left(\cosh \frac{X_m}{\lambda} - 1\right)$$

$$= \lambda C \tanh\left(\frac{X_m}{2\lambda}\right)$$

which agrees with the other approach on p. 131 for W
cf also p. 133

e.g. $X_m = 1\,mm$, $C = 1\,mV/mm$

$\lambda_1 = 1\,mm$, giving $Z_m = 1$ $\quad V_0 = 1 \cdot \tanh(0.5) = 0.462\,mV$
$\lambda_1 C = 1\,mV$

$\lambda_2 = 0.2\,mm$, giving $Z_m = 5$ $\quad V_0 = (0.2)\tanh(2.5) = \frac{.9866}{5}$
$\lambda_2 C = 0.2\,mV$ $\quad = .1973\,mV$

For long axons parallel to applied field of infinite length, we have that $\tanh\left(\frac{X_m}{2\lambda}\right) = 1$ for all and hence, $V_0 = \lambda C$ and hence that effectiveness of stimulus $\propto \lambda \propto \sqrt{d}$ for some materials

However, for neurons of finite extent, the tanh term comes in too

4/14/65

The interpretation here is that for same lengths & same $\frac{dF}{dx}$, the shorter λ $\left\{ \begin{array}{l} \text{either smaller } R_m/R_i \\ \text{or smaller diameter} \end{array} \right.$

gets a larger penetration of current into core in the sense that the current density in the core & hence the IR drop in the core is increased to become closer to the applied gradient.

The result is that the depol & hyperpol of the ends is reduced. Bear in mind that this is the steady state, we have not said how long this takes. Presumably, with the smaller λ & ~~the greater penetration~~, it takes longer to reach st. st.? Notice that earliest part of transient goes thru C_m & sets up full applied gradient inside, very briefly, but then one can view the depol & hyperpol. as the development of bucking potentials.

Question, how to get the most from a given $\frac{dF}{dx} = C$

Answer must be for $\tanh\left(\frac{Z_m}{2}\right) \doteq 1$

and λ maximized

In other words, a cylinder of infinite length with largest possible λ

Then $V(-\infty) \rightarrow \lambda C$, in other words, the bigger the better

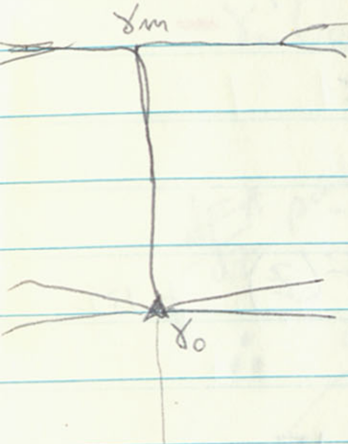
see also p. 138 of Book 9 for finite length, true, the larger λ the better

and if half length, h, is $< \frac{\lambda}{4}$

get depol $= hC$

4/15/65 Now wish to examine effects of γ_0 and γ_m factors governing nonzero slopes at ~~Z~~ $Z=0$ & Z_m

γ_0 already treated in old notes 5/18/61



γ_0 would refer to basal dendrites $\perp$ to ∇V_e

γ_m would refer to ~~ends of~~ apical tufts that lie $\perp$ to ∇V_e

Here we have $\dfrac{dU}{dZ} = \gamma_0 U_0 = \gamma V_0$ at $Z=0$

$$\frac{dU}{dZ} = \gamma_m(-V_m) = -\gamma_m(U_m - F_m) \quad \text{at } Z = Z_m$$

As before DE is $\dfrac{d^2U}{dZ^2} - U = -F(Z)$

Laplace transform to get $s^2 u - sU_0 - \gamma_0 U_0 - u = -f$

B.C. at $Z=0$

Therefore $$u = U_0\left(\frac{s+\gamma_0}{s^2-1}\right) - \frac{f}{s^2-1}$$

giving $$U(Z) = U_0\{\cosh Z + \gamma_0 \sinh Z\} - F^* \sinh Z$$

$$\frac{dU}{dZ} = U_0\{\sinh Z + \gamma_0 \cosh Z\} - F^* \cosh Z$$

which already satisfies B.C. at $Z=0$, Now for $Z = Z_m$

$$-\gamma_m(U_m - F_m) = U_0\{\sinh Z_m + \gamma_0 \cosh Z_m\} - \left[F^* \cosh Z\right]_{Z=Z_m}$$

Now $$U_m = U_0\{\cosh Z_m + \gamma_0 \sinh Z_m\} - \left[F^* \sinh Z\right]_{Z=Z_m}$$

$$\equiv \; -\left[\frac{dF^*}{dZ}\cosh Z - F\right]_{Z=Z_m}$$ See p.132

$$\therefore \gamma_m(U_m - F_m) = \gamma_m U_0\{\cosh Z_m + \gamma_0 \sinh Z_m\} - \gamma_m\left[\frac{dF^*}{dZ}\cosh Z\right]_{Z=Z_m}$$

Thus we eliminate U_m and F_m

go to next page

The ~~general~~ complete solution for all these V_0 can be expressed

$$U(Z) = V_0 \{ \cosh Z + \gamma_0 \sinh Z \} - F^* \sinh Z$$

also, using that $-F^* \sinh Z = -\frac{dF}{dZ}^* \cosh Z + F(Z)$ p. 132
we can write that $(V_0 = U_0)$

$$V(Z) = U - F = V_0 \{ \cosh Z + \gamma_0 \sinh Z \} - \frac{dF}{dZ}^* \cosh Z$$

Now, $\boxed{\text{for } F = bZ}$ got $F^* \sinh Z = b \sinh Z - bZ$

giving $V(Z) = U - F = V_0 \{ \cosh Z + \gamma_0 \sinh Z \} - b \sinh Z$
$= V_0 \cosh Z + (\gamma_0 V_0 - b) \sinh Z$

Also $\frac{dF}{dZ} = b$

Hence $\left(F + \gamma_m \frac{dF}{dZ}\right)^* \cosh Z = (bZ + \gamma_m b)^* \cosh Z$

$$= b \int_0^Z (\tau + \gamma_m) \cosh (Z - \tau) \, d\tau$$

$$= b \int_0^Z (Z - \tau + \gamma_m) \cosh (\tau) \, d\tau$$

$$= b \Big[(Z - \tau + \gamma_m) \sinh \tau \Big]_0^Z - b \int_0^Z (-1) \sinh \tau \, d\tau$$

$$= b \{ + \gamma_m \sinh Z + \cosh Z - 1 \}$$

When $Z = Z_m$, this gives numerator of general expression at sight

4/15/65

From previous page, elimination of U_m and F_m leads to the condition

$$-\gamma_m U_0\{\cosh Z_m + \gamma_0 \sinh Z_m\} + \gamma_m\left[\frac{dF}{dZ} * \cosh Z\right]_{Z=Z_m} = U_0\{\sinh Z_m + \gamma_0 \cosh Z_m\} - \left[F^* \cosh Z\right]_{Z=Z_m}$$

$\frac{dF}{dZ}^* \sinh Z$

$$\therefore U_0 = \frac{\left[F^* \cosh Z\right]_{Z=Z_m} + \gamma_m\left[\frac{dF}{dZ}^* \cosh Z\right]_{Z=Z_m}}{\sinh Z_m + \gamma_0 \cosh Z_m + \gamma_m\{\cosh Z_m + \gamma_0 \sinh Z_m\}}$$

For the case, $\gamma_m = 0$, this reduces simply to

$$U_0 = \frac{\left[F^* \cosh Z\right]_{Z=Z_m}}{\sinh Z_m + \gamma_0 \cosh Z_m}$$

in agreement with page 2 of 6/7/61 notes

For the case, $\gamma_0 = 0 = \gamma_m$, this reduces to earliest case

$$U_0 = \frac{\left[F^* \cosh Z\right]_{Z=Z_m}}{\sinh Z_m}$$

For the case, $\gamma_0 = 0$ but $\gamma_m > 0$, we obtain

$$U_0 = \frac{\left[\cosh Z * \left(F + \gamma_m \frac{dF}{dZ}\right)\right]_{Z=Z_m}}{\sinh Z_m + \gamma_m \cosh Z_m}$$

alternative numerator is $\left[\frac{dF}{dZ} * (\sinh Z + \gamma_m \cosh Z)\right]_{Z=Z_m}$

The general result can be most compactly expressed as

$$U_0 = \frac{\left[\cosh Z * \left(F + \gamma_m \frac{dF}{dZ}\right)\right]_{Z=Z_m}}{(1 + \gamma_0\gamma_m)\sinh Z_m + (\gamma_0 + \gamma_m)\cosh Z_m}$$

For case (1) of p 137 $\quad b = 1$ mV per λ , $Z_m = 1$

$$\tanh\left(\frac{Z_m}{2}\right) = 0.462$$

$$\coth(Z_m) = \frac{1}{.762} = 1.313$$

$$\therefore U_0 = V_0 = \frac{0.462 + \gamma_m}{1 + 1.31\,\gamma_m}$$

if $\gamma_m = 1$, get $\frac{0.462 + 1.0}{1 + 1.31} = \cancel{0.538} = \frac{1.462}{2.31} = 0.63$

$\gamma_m = 2$ gives $\frac{2.462}{3.62} = 0.68$

as $\gamma_m \to \infty$, $U_0 = V_0 \to \frac{1}{1.31} = 0.76$

$\gamma_m = 3$ gives $\frac{3.462}{4.93} = 0.70$

For case (2) of p. 137 get $(0.2)\left(\frac{.9866 + \gamma_m}{1 + 10\gamma_m}\right)$

and for $\gamma_m = 1$, get $\frac{1.9866}{10} = 0.19866$

which is almost unchanged

No value of γ_m can have much effect

General expression for $U_0 = V_0$ can be rearranged to read

$$\boxed{U_0 = V_0 = b\tanh\left(\frac{Z_m}{2}\right)\left\{\frac{1 + \gamma_m\coth\left(\frac{Z_m}{2}\right)}{1 + \gamma_0\gamma_m + (\gamma_0 + \gamma_m)\coth(Z_m)}\right\}}$$

4/15/65

Thus from pp 141–143 we get for $F = bZ$

That $$U_0 = V_0 = \frac{b\{\cosh Z_m - 1 + \gamma_m \sinh Z_m\}}{(1 + \gamma_0\gamma_m)\sinh Z_m + (\gamma_0 + \gamma_m)\cosh Z_m}$$

see lower left p. 144

and that $V(Z) = V_0\{\cosh Z + \gamma_0 \sinh Z\} - b \sinh Z$

For special case of $\gamma_0 = 0$, this reduces to

$$U_0 = V_0 = \frac{b\{\cosh Z_m - 1 + \gamma_m \sinh Z_m\}}{\sinh Z_m + \gamma_m \cosh Z_m}$$

which can also be expressed ~~as~~ by dividing numerator & denom by $\sinh Z_m$

$$U_0 = V_0 = b\left\{\frac{\tanh\left(\frac{Z_m}{2}\right) + \gamma_m}{1 + \gamma_m \coth(Z_m)}\right\}$$

which reveals most clearly, the effect of γ_m See left

To agree with page 137, this can also be written

$$U_0 = V_0 = \lambda C\left\{\frac{\tanh\left(\frac{X_m}{2\lambda}\right) + \gamma_m}{1 + \gamma_m \coth\left(\frac{X_m}{\lambda}\right)}\right\}$$

where $\frac{dF}{dX} = C$ and $\lambda = \text{const.}$

Sign error caught just at this pt.

~~* what is the physical meaning of a zero denominator?~~

for $\gamma_m = 0$ get $\lambda C \tanh\left(\frac{X_m}{2\lambda}\right)$

This shifts the midpoint of symmetric case to the Z_m end.

as $\gamma_m \to \infty$, answer approaches $\lambda C \tanh\left(\frac{X_m}{\lambda}\right)$

i.e. not quite a doubling

following p.147 & 143 now do $\cosh Z * \left(F + \gamma_m \frac{dF}{dZ}\right)$

$$F + \gamma_m \frac{dF}{dZ} = \frac{b}{a}\left(1 - e^{-aZ}\right) + \gamma_m \frac{b}{\cancel{a}}\left(\cancel{a}e^{-aZ}\right)$$

$$= \frac{b}{a}\left[1 + (a\gamma_m - 1)e^{-aZ}\right] = \frac{b}{a}\left[1 - (1 - a\gamma_m)e^{-aZ}\right]$$

Laplace transform is of convolution $\frac{b}{a}\left(\frac{1}{s} - \frac{1 - a\gamma}{s+a}\right)\left(\frac{s}{s^2-1}\right) = \frac{b}{a}\left(\frac{1}{s^2-1} - \frac{s(1-a\gamma)}{(s+a)(s^2-1)}\right)$

$$= \frac{b}{a}\left(\frac{a + a\gamma s}{(s+a)(s+1)(s-1)}\right)$$

for $\frac{A}{s+1} + \frac{B}{s-1} + \frac{C}{s+a}$, want $\frac{s(A+B) - A + B}{(s^2-1)} + \frac{C}{(s+a)}$

get $A = \frac{a\gamma - a}{2(a-1)}$, $B = \frac{a\gamma + a}{2(a+1)}$, $C = \frac{-a(a\gamma - 1)}{a^2-1}$

get $\left(\frac{b}{a^2-1}\right)\left(\frac{(a\gamma - 1)s}{s^2-1} + \frac{a^2 - a\gamma}{a(s^2-1)} - \frac{(a\gamma - 1)}{s+a}\right)$

yields $\left(\frac{b}{a^2-1}\right)\left\{(a - \gamma)\sinh Z - (1 - a\gamma)\cosh Z + (1 - a\gamma)e^{-aZ}\right\}$

Which can also be obtained from lower right.

∴ Can express $U_0 = V_0$ for $\gamma_0 + \gamma_m$ refer to p.143

$$\boxed{U_0 = \left(\frac{b}{1-a^2}\right)\frac{\left[(1 - a\gamma_m)\cosh Z_m - (1 - a\gamma_m)e^{-aZ_m} - (a - \gamma_m)\sinh Z_m\right]}{(1 + \gamma_0\gamma_m)\sinh Z_m + (\gamma_0 + \gamma_m)\cosh Z_m}}$$

See p.148

alternate method uses inset page for numerator

$\rightarrow \frac{dF}{dZ} * (\sinh Z + \gamma_m \cosh Z)$

by multiplying $\{\ \}$ expression by $(1 - ab\gamma_m)$

4/15/65

Simpler evaluation

for $a^2 \neq 1$

$$\phi^* \cosh z = \frac{df}{dz}^* \sinh z$$

$$= b\int_0^z e^{-ay}\cosh(z-y)\,dy$$

$$= \frac{b}{2}e^{z}\int_0^z e^{-(1+a)y}\,dy + \frac{b}{2}e^{-z}\int_0^z e^{(1-a)y}\,dy$$

$$= \frac{b}{2}e^{z}\left[\frac{e^{-(1+a)z}-1}{-(1+a)}\right] + \frac{b}{2}e^{-z}\left[\frac{e^{(1-a)z}-1}{1-a}\right]$$

$$= \frac{b}{2(a^2-1)}\left\{(1-a)\left(e^{-az}-e^{z}\right) - (1+a)\left(e^{-az}-e^{-z}\right)\right\}$$

$$= \frac{b}{(a^2-1)}\left\{e^{-az} - \cosh z + a\sinh z\right\}$$

Q.E.D.

Similarly $\frac{df}{dz}^* \cosh z =$

$$\frac{b}{(a^2-1)}\left\{-ae^{-az} - \sinh z + a\cosh z\right\}$$

for $a=1$ get for $\phi^* \cosh z$

$$\frac{b}{2}e^{z}\left(\frac{e^{-2z}-1}{-2}\right)-\frac{b}{2}ze^{-z}$$

$$=\frac{b}{2}\left(\frac{e^{z}-e^{-z}}{2}\right)-\frac{b}{2}ze^{-z}$$

$$=\frac{b}{2}\left\{\sinh z-ze^{-z}\right\}$$

4/15/65

Now consider $F(Z) = \frac{b}{a}\left(1 - e^{-aZ}\right)$

and possibly also $\frac{dF}{dx} = C$, $\left\{ \frac{dZ}{dx} = e^{\alpha x} \equiv \frac{dx}{dZ} = e^{-\alpha x} \right\}$

This case was solved in the 6/5/61, 6/7/61 notes

$U_0 = V_0$ requires $\left[F^* \cosh Z \right]_{Z=Z_m}$ for $\gamma_m = 0$

old method was $L_1\left\{ \frac{b}{a}\left(1-e^{-aZ}\right) * \cosh Z \right\} = \frac{b}{a}\left(\frac{1}{s} - \frac{1}{s+a}\right)\left(\frac{s}{s^2-1}\right)$

$= b\left(\frac{\cancel{s}\,1}{(s+a)(s^2-1)}\right)$

$= \left(\frac{b}{1-a^2}\right)\left(\frac{s}{s^2-1} - \frac{a}{s^2-1} - \frac{1}{s+a}\right) \rightarrow \checkmark$

$\therefore$ get $F^* \cosh Z = \left(\frac{b}{1-a^2}\right)\left(\cosh Z - a\sinh Z - e^{-aZ}\right)$

note that as $a \to 0$, this $\to b(\cosh Z - 1)$, as it should

Directly $F^* \cosh Z = \frac{b}{a}\int_0^Z \cosh \tau \left(1 - e^{-a(Z-\tau)}\right) d\tau$

$= \frac{b}{a}\int_0^Z \cosh \tau \, d\tau - \frac{b}{2a}\int_0^Z \left(e^{\tau - aZ + a\tau} + e^{-\tau - aZ + a\tau}\right) d\tau$

$= \frac{b}{a}\left[\sinh \tau\right]_0^Z - \frac{b}{2a}\left[\left(e^{-aZ}\right)\left(\frac{e^{(a+1)\tau}}{a+1}\right) + \left(e^{-aZ}\right)\left(\frac{e^{(a-1)\tau}}{a-1}\right)\right]_0^Z$

$= \frac{b}{a}\sinh Z - \frac{b}{2a}\left\{\frac{e^{Z} - e^{-aZ}}{a+1} + \frac{e^{-Z} - e^{-aZ}}{a-1}\right\}$

$= \frac{b}{a}\sinh Z - \frac{b}{2a(a^2-1)}\left\{a\left(e^{Z} + e^{-Z}\right) - 2ae^{-aZ} + \left(e^{Z} - e^{-Z}\right)\right\}$

$= \left(\frac{b}{a^2-1}\right)\left\{\left(\frac{a^2-1}{a}\right)\sinh Z - \cosh Z + e^{-aZ} + \frac{1}{a}\sinh Z\right\}$

$= \left(\frac{b}{a^2-1}\right)\left\{a\sinh Z - \cosh Z + e^{-aZ}\right\}$

QED

for $\gamma_0 = 0 = \gamma_m$ result on p. 146 reduces to

$$V_0 = \left(\frac{b}{1-a^2}\right)\left(\coth Z_m - a - \frac{e^{-aZ_m}}{\sinh Z_m}\right)$$

for $\gamma_0 = 0$ but $\gamma_m \geqq 0$, get

$$V_0 = \left(\frac{b}{1-a^2}\right)\left(\frac{(1-a\cancel{b}\gamma_m)\coth Z_m - a + \cancel{b}\gamma_m - (1-a\cancel{b}\gamma_m)\frac{e^{-aZ_m}}{\sinh Z_m}}{1+\gamma_m \coth Z_m}\right)$$

and for γ_0 & γ_m both > 0 get

$$V_0 = \left(\frac{b}{1-a^2}\right)\left(\frac{\text{same numerator}}{1+\gamma_0\gamma_m + (\gamma_0+\gamma_m)\coth Z_m}\right)$$

as $\gamma_m \to \infty$, limiting expression is

$$V_0 = \left(\frac{b}{1-a^2}\right)\left[-ab + b\tanh Z_m + ab\left(\frac{e^{-aZ_m}}{\cosh Z_m}\right)\right]$$

4/15/65

Note that if $\frac{dF}{dx} = c$ and $\frac{dx}{dZ} = e^{-\alpha x}$

$$\frac{dZ}{dx} = e^{\alpha x}, \quad Z_2 - Z_1 = \int_{x_1}^{x_2} e^{\alpha x}\, dx = \left[\frac{e^{\alpha x}}{\alpha}\right]_{x_1}^{x_2} = \frac{e^{\alpha x_2} - e^{\alpha x_1}}{\alpha}$$

and, starting from $x = 0$, we would have $Z = \frac{e^{\alpha x} - 1}{\alpha}$

Then $e^{\alpha x} = \alpha Z + 1$ and $e^{-\alpha x} = \frac{1}{\alpha Z + 1}$

$$\therefore \frac{dF}{dZ} = \frac{dF}{dx}\frac{dx}{dZ} = \frac{c}{\alpha Z + 1}$$

It is remarkable that Laplace transforms are not given for $\frac{a}{t+b}$ or for $\log(t+b)$

e.g. would need $\int_0^\infty \frac{a e^{-st}}{t+b}\, dt$ This integral is obviously finite, but there does not seem to be a conventional closed form for this.

note that $\int \frac{e^{ax}}{x}\, dx = \log x + \frac{ax}{1} + \frac{a^2x^2}{2\cdot 2!} + \frac{a^3x^3}{3\cdot 3!} + \ldots$

$\therefore$ better to use $\frac{dF}{dZ} = b e^{-aZ}$ as on previous page

This implies that $\frac{dZ}{dx} = \frac{c}{b} e^{aZ}$ for $\frac{dF}{dx} = c$

$$= \frac{c}{b} \exp\{b - b e^{-aZ}\}$$

cannot get expression in terms of x

But, in last analysis, do not really need it.

$$\frac{dx}{dZ} = e^{-aZ}, \quad x = \frac{1}{a}(1 - e^{-aZ}) \quad \text{where } x = \frac{X}{\lambda_0}$$

From Table I of N.Y.acad.

Z	X/λ_0	Cost offset approx	$\frac{1}{3}(1-e^{-3Z})$	$\frac{1}{2}(1-e^{-2Z})$	$(1-e^{-Z})$
0	0		0	0	0
.1	.1	.1	.09	.09	.10
.2	.18	.15	.15	.165	.18
.4	.31	.25	.23	.275	.33
.6	.41	.30	.26	.35	.45
.8	.49	.34	.30	.40	.55
1.0	.55	.35	.32	.42	.63

$= 1 - e^{-}$

limiting expression as $\gamma_m \to \infty$ is

$$\left(\frac{-1}{8}\right)\left(-3 + 0.762 + 3\left(\frac{.05}{1.543}\right)\right)$$
$$.097$$

$$\begin{array}{r} -3.0 \\ +.859 \\ \hline 2.14 \end{array}$$

$$= \left(\frac{-1}{8}\right)(-2.14)$$

$$= +0.267$$

Comment. This $\frac{dx}{dZ} = e^{-aZ}$ effect applies to motoneurones but not nearly so much, if at all, to apical dendrite. For latter, better to use earlier (p. 144) result.

4/15/65

Calc. for $b = 1$ mv per λ, $Z_m = 1$, $a = 3$, $\gamma_0 = 0$

$\gamma_m = 0$

found to approx in 1961 the N.Y. Acad. neurone

Then later $\gamma_m = 2$

from p. 148

get $V_0 = \left(\frac{1}{1-9}\right)\left(\coth(1) - 3 - \frac{e^{-3}}{\sinh(1)}\right)$

$= \left(\frac{1}{8}\right)\left(3.0 + \frac{.05}{1.175} - 1.313\right)$

$$\begin{array}{r} 3.043 \\ -1.313 \\ \hline 1.730 \end{array}$$

$= \frac{1.73}{8} = 0.216$ which agrees with 1961 calc. 6/5/61 for $\gamma_0 = 0$

This is roughly half of that obtained for $a = 0$ i.e. linear core .462

Now, set $\gamma_m = 2$ fortunately $b = 1$ & did not get error here

get $V_0 = \left(\frac{1}{1-9}\right)\left(\frac{(1-3\cdot 2)\coth(1) - 3 + 2 - (1-3\cdot 2)\left(\frac{.05}{1.175}\right)}{1 + 2\coth(1)}\right)$

$= \left(\frac{1}{-8}\right)\left(\frac{(-5)(1.313) - 1 - (-5)(.043)}{1 + 2.626}\right)$

$$\begin{array}{r} 1.313 \\ +\ .2 \\ \hline 1.513 \\ -\ .043 \\ \hline 1.470 \end{array}$$

$= \left(\frac{5}{8}\right)\left(\frac{1.47}{3.626}\right) = \frac{7.34}{8(3.626)}$

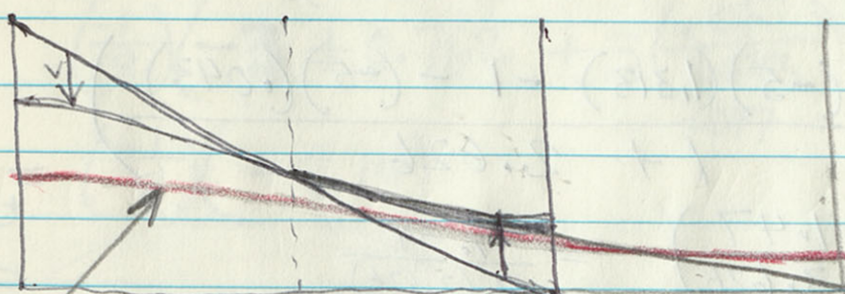
$= \frac{2.03}{8} = 0.254$

approx 20% increase

This figures, because, since $\frac{dF}{dZ}$ falls off toward periphery, change slope factor should have less effect.

Whereas on p. 144, for $\frac{dF}{dZ}$ const got approx 50% increase

Reversed F(Z) & F(Z')



shifted U, more hyperpol.

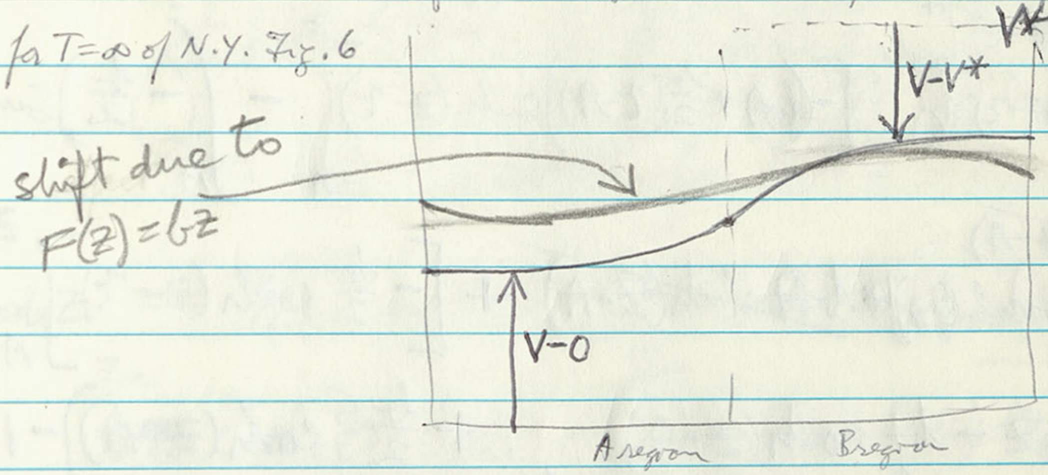
Qualitatively, the effect is similar to γ_m effect

4/16/65

Should try to write this up briefly, but first consider two more points ① Calc max. effect for a small neuron

② Theory for two region neuron of NY, Acad Paper.

e.g. for $T=\infty$ of N.Y. Fig. 6



But, more particularly, if A region is normal and B region has J with $E_j = E_r$

Then $V^* = 0$ in both regions

and the only difference between A region & B region is that $k_b > 1$

$k_a = 1$

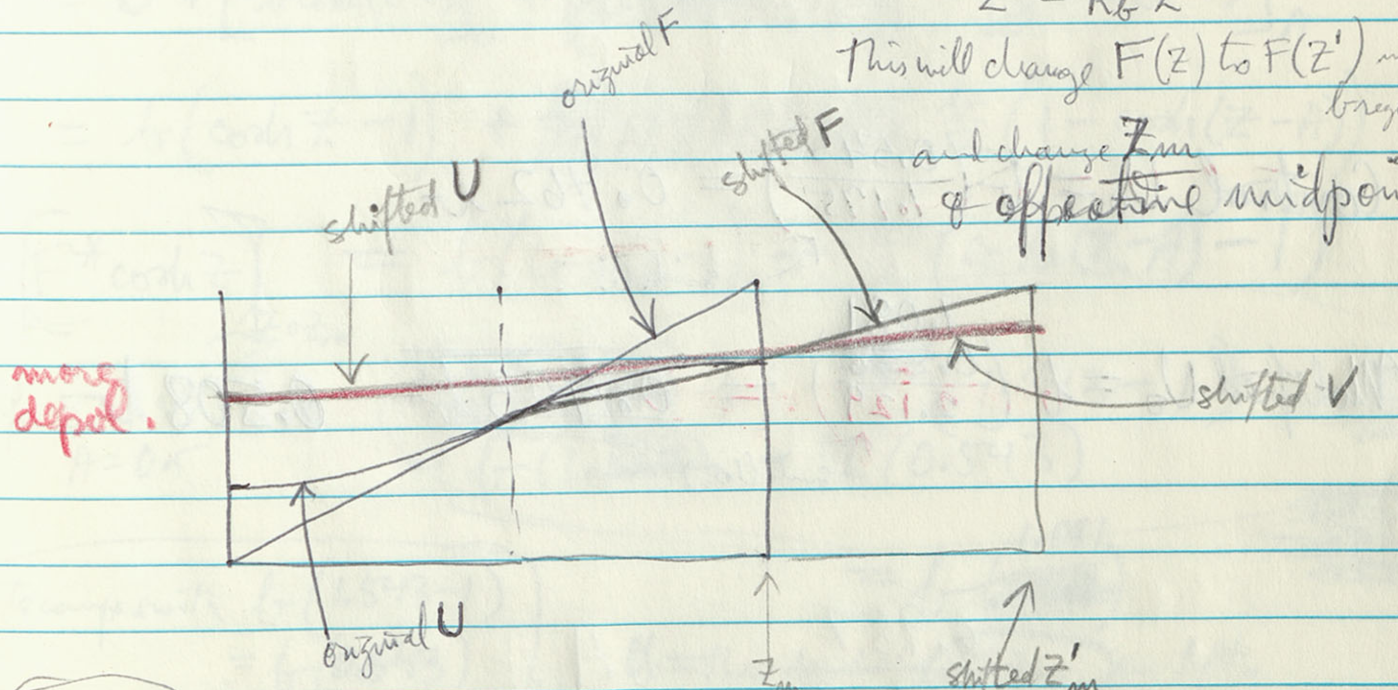
This can be handled most easily by redefining Z in B region

$Z' = k_b Z$

This will change $F(Z)$ to $F(Z')$ in B region

and change Z_m

& effective midpoint



for $k_b = 2$

i.e. $F(Z')$ has one slope in A region & half slope in B region

OK now. Originally made mistake of setting first integral equal to $b\{b\cosh A - 1\}$, which was incorrect

$$\int_0^A b\tau \cosh(Z-\tau)\,d\tau + \int_A^Z \left[bA + \frac{b}{2}(\tau - A)\right]\cosh(Z-\tau)\,d\tau$$

$$= \left[b\tau \sinh(Z-\tau)\right]_0^A - \int_0^A -b \sinh(Z-\tau)\,d\tau \quad \left[-\left(bA + \frac{b}{2}(\tau-A)\right)\sinh(Z-\tau)\right]_A^Z - \int_A^Z \left(-\frac{b}{2}\right)\sinh(Z-\tau)\,d\tau$$

$$= \cancel{-bA\sinh(Z-A)}$$
$$+ b\cosh Z - b\cosh(Z-A) + \cancel{bA\sinh(Z-A)} + \left[-\frac{b}{2}\cosh(Z-\tau)\right]_A^Z$$

$$= b\cosh Z - b\cosh(Z-A) + \frac{b}{2}\{\cosh(Z-A) - 1\}$$

$$= b\cosh Z - \frac{b}{2}\cosh(Z-A) - \frac{b}{2}, \text{ which agrees with result at right.}$$

$A = 0.5$
$Z = 1.5$

$$= b(2.352) - \frac{b}{2}(1.543 + 1)$$

$2 \,|\, 2.543$
1.271

$$= b\{2.352 - 1.271\}$$
$$= b\{1.081\}$$

✓

$$\text{Control } U_0 = b\left(\frac{0.543}{1.175}\right) = 0.462\,b$$

sinh(1)

$$\text{Modified } U_0 = b\left(\frac{1.081}{2.129}\right) = \cancel{0.403\,b} \quad 0.508\,b$$

sinh(1.5)

4/16/65 Calc $F * \cosh Z$ for $\frac{dF}{dZ} = \begin{cases} b & \text{for } 0 \le Z \le A \\ \frac{b}{2} & \text{for } A \le Z \le Z_m \end{cases}$

or $F = \begin{cases} bZ & \text{for } 0 \le Z \le A \\ bA + \frac{b}{2}(Z-A) & \text{for } A \le Z \le Z_m \end{cases}$

Try
$A = 0.5$
$Z_m = 1.5$

or $bZ - \frac{b}{2}(Z-A)$ for $A \le Z \le Z_m$

$\therefore F * \cosh Z = \frac{dF}{dZ} * \sinh Z + F(0) \sinh Z$

See p. 132 can be sought in several ways

one way is $\int_0^{Z_m} b\tau \cosh(Z-\tau)\,d\tau - \int_A^{Z_m} \frac{b}{2}(\tau - A)\cosh(Z-\tau)\,d\tau$

$= \left[-b\tau \sinh(Z-\tau)\right]_0^{Z_m} - \int_0^{Z_m} -b \sinh(Z-\tau)\,d\tau - \left[\frac{b}{2}(\tau-A)\sinh(Z-\tau)\right]_A^{Z_m} + \int_A^{Z_m} -\frac{b}{2}\sinh(Z-\tau)\,d\tau$

$= 0 + \left[-b\cosh(Z-\tau)\right]_0^{Z} + 0 + \left[\frac{b}{2}\cosh(Z-\tau)\right]_A^{Z_m}$

$= b(\cosh Z - 1) + \frac{b}{2}(1 - \cosh(Z-A))$

$\left[F * \cosh Z\right]_{Z=Z_m} = b(\cosh Z_m - 1) - \frac{b}{2}(\cosh(Z_m - A) - 1)$

for $Z_m = 1.5$, $A = 0.5$

$= b(2.352 - 1) - \frac{b}{2}(1.543 - 1)$

$= b(1.352) - \frac{b}{2}(0.543)$

$= b(1.081)$

1.352
−.271
1.081

~~1.129~~
~~−.271~~
~~.858~~

To compare with $b(1.543 - 1)$
$= b(0.543)$
for $Z_m = 1.0$
and $\frac{dF}{dZ} = b$ all the way

$U_0 =$ these divided by $\sinh Z_m$, see left.

This confirms expectation of shift as sketched at bottom of page 153.

See p. 165 for Electric Field paper

4/16/65

Visited Reese + Brightman's display as planned for Miami anatomy meetings next week.

They asked me to go thru my reasoning for them again. One interesting development is that the synapses that we ~~want~~ use for ~~sustained~~ I have the largest number of vesicles handy, also, they have less postsynaptic web + are more similar to presumed inhibitory synapses (axo-somatic) elsewhere. Brightman was worried about short-circuiting of two neighboring synapses, but this is taken care of first by time sequence.

Tom phoned back at 5:30 PM. He was concerned about two points in particular. (1) Salmoraghi's blocking of adrenergic transmitters + thus blocking mitral inhibition might provide a means to ~~find~~ locate which ~~of~~ these dendrodendritic jcns is adrenergic; he lent me a reprint to look. My main reaction is that to look for effect on granule field, must be blocking population, not individual. This may be possible.

(2) I admitted to being uncertain if granule field lasts as long as the inhibition. Must write Gordon to see if he has evidence that field lasts longer when inhib. lasts longer? It is my impression that the two effects start together.

Reese + Brightman both very much concerned to have a good physiol. argument, because otherwise the anatomists would be extremely skeptical.

If $j = t$ at terminal branch point — Look at p. 501 of 1959 paper

$$C_j = \sum_k C_{jk} \left[d_{jk} / d_{j+1} \right]^{3/2}$$

$$C_t = \cancel{B_t} + \left(\frac{d_{t-1}}{d_t}\right)^{3/2} \left\{ \frac{C_{t-1} + \tanh Z_{t-1}}{1 + C_{t-1} \tanh Z_{t-1}} \right\} \cancel{+ B_t}$$

was OK

And, in general, $C_j = B_j + \left(\frac{d_{j-1}}{d_j}\right)^{3/2} \left\{ \frac{C_{j-1} + \tanh Z_{j-1}}{1 + C_{j-1} \tanh Z_{j-1}} \right\}$

from Table I $\quad C_t = 0.32 + \left(\frac{1}{.54}\right)\left(\frac{C_{t-1} + 0.26}{1 + 0.26\, C_{t-1}}\right)$

If $C_{t-1} = 1.0$, get $C_t = 0.32 + 1.85 = 2.17$

Must work from soma, to get the C_{j-1} values

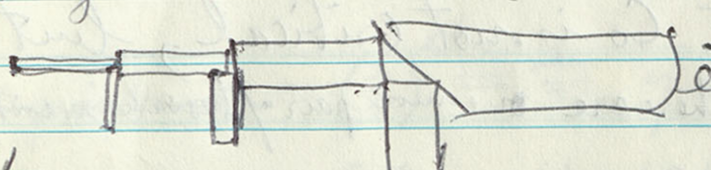
4/19/65

Tom Reese still in town. I had Dorothy type a final typing of my rough 4/9/65 draft of memo outlining the physiol. argument, and gave this to Tom before he left for the meeting. He pointed out the amacrine cells of fig. 191 on page 308 of Cajal as being possibly very similar in mammalian retina, to our granule cells in bulb. Also, he showed me a Xerox of a paper by Hirata (Arch. Histol. Jap. — Vol. 24, p. 293–302 (1964) which reports the same structures that Tom & Milton report, but without identification of the pathway.

4/20/65 completed annual report. Corrected errors on p. 154, 155

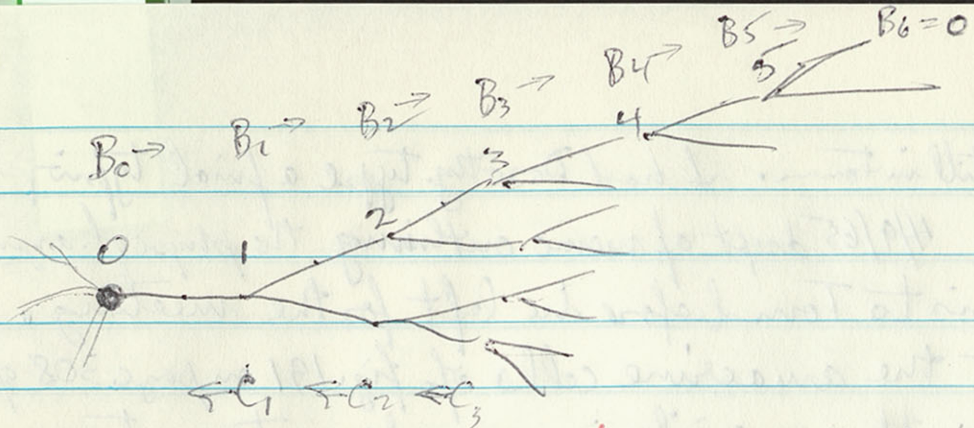
4/21/65 finally wrote long letter to Gordon, got off "pink" travel request, and letter to Lamport, acknowledging his note.
Phone call from Don Pollen & Dieter Lux who wish to see me ~~next day~~ soon. Agreed next day.

4/22/65 Last night, happened to think that spread from synaptic input to single twig could be dealt with, at least approx, by using $K \neq 0$ of N.Y. Acad paper. Then the G input from twig can be seen to be larger than I believe (must recheck) Katz had thought.
J. Physiol 1963 Vol 168 p. 419



~~See left.~~

Let C_j be reverse direction to B_j of ~~N.~~ 1959 paper
If radially out from soma, $\Sigma d^{3/2}$ = const at each branch,
Then, for N.Y. acad neuron, from twig in, $\Sigma d^{3/2}$ jumps up by factor of 3 at each branch point, although earlier side branches are short.



$\leftarrow C_0 = 3.83$

$$C_1 = B_1 + 2\left\{\frac{C_0 + \tanh Z_0}{1 + C_0 \tanh Z_0}\right\}$$

This was ok because here, $B_j = B_{jk}$, because of equal branching with $\Sigma d^{3/2}$ preserved.

But see p. 163

This time, suppose $C_0 = 10 B_0 = 7.66$

$$C_1 = 0.72 + 2\left\{\frac{7.66 + .1}{1.766}\right\} = 0.72 + 2(4.4) = 9.5$$

$$C_2 = 0.67 + 2\left\{\frac{9.6}{1.96}\right\} = 0.67 + 2(4.9) = 10.5$$

$$C_3 = 0.54 + 2\left(\frac{10.7}{3.1}\right) = 0.54 + 2(3.45) = 7.44$$

$$C_4 = 0.38 + 2\left(\frac{7.64}{2.05}\right) = 0.38 + 2(3.05) = 6.48$$

$$C_5 = 0.2 + 2\left(\frac{6.8}{2.3}\right) = 0.2 + 2(2.91) = 6.02$$

$$C_6 = 0 + \frac{6.22}{2.02} \longrightarrow 2.83$$

Thus it is clear that C_0 is not critical, but Z is.

~~Suppose Z_0~~ Suppose there are one more pair of branches with $Z_6 = .1$

Then $C_6 = 0.1 + 2(2.83) = 5.76$

and $C_7 = 0 + \frac{5.86}{1.58} = 3.71$ which is larger than

but in a smaller branch

4/22/65 Calc B_j and then C_j for the N.Y. Acad. Neurone

j		B_{j+1}	Z_j	$\tanh Z_j$	$B_{jk} = B_j$
5	Quin	0	0.2	≈0.2	$\frac{0+0.2}{1} = 0.2 = B_5$
4	Quat	0.2	0.2	~0.2	$\frac{0.2+0.2}{1+.04} = 0.384 = B_4$
3	~~Tert.~~	0.384	0.2	~0.2	$\frac{0.584}{1.077} = 0.542 = B_3$
2	Sec	0.542	0.2	~0.2	$\frac{0.742}{1.108} = 0.669 = B_2$
1	Prim	0.67	0.1	~0.1	$\frac{0.77}{1.07} = 0.72 = B_1$
0	Trunk	0.72	0.1	~0.1	$\frac{0.82}{1.07} = 0.766 = B_0$

Now, reverse direction & use — see previous page

see left $$C_j = B_j + 2\left\{\frac{C_{j-1} + \tanh Z_{j-1}}{1 + C_{j-1}\tan Z_{j-1}}\right\}$$

~~because B_j refers to d_{j-1} diameter, while C_j refers to d_j diameter~~

Suppose that $G_{\text{soma + all dendrite except one tree}}^{p\to\infty} = 5 \times G_{\text{prim tree}}$

for $p\to\infty$, want (N-1)

Then $C_0 = 5 * B_0 = 3.83$

$C_1 = 0.72 + 2\left\{\frac{3.83+.1}{1+.383}\right\} = 0.72 + (2.84)\times 2 \; (5.68) = 6.4$

$C_2 = 0.67 + 2\left\{\frac{6.4+.1}{1.64}\right\} = 0.67 + 2(3.97) = 8.61$

$C_3 = 0.54 + 2\left\{\frac{8.61+.2}{1+1.72}\right\} = 0.54 + 2(3.24) = 7.02$

$C_4 = 0.384 + 2\left\{\frac{7.02+.2}{1+1.4}\right\} = 0.384 + 2(3.01) = 6.40$

$C_5 = 0.2 + 2\left\{\frac{6.4+.2}{1+1.28}\right\} = 0.2 + 2(2.90) = 6.0$

$C_6 = 0 + \frac{6.0+0.2}{1+1.2} = \frac{6.2}{2.2} \longrightarrow 2.82$

G_∞ in quin. branch $= \left(\frac{1}{2}\right)^5 = \frac{1}{32}$ of G_∞ in trunk

$\therefore \frac{\text{Terminal input } G}{\text{Trunk input } G} = \left(\frac{1}{32}\right)\left(\frac{2.82}{0.77}\right) = \frac{3.67}{32} = 0.115$

$\frac{\text{Terminal input } G}{\text{Whole neuron input } G} \simeq \frac{0.115}{6.0} \approx 0.02$ which is close to what Katz & Miledi said on p. 419 of J. Physiol 168 (1963). See p. 163 bottom

Approx

$G_N/G_{0\infty} = 4.6$	$G_N/G_N = 1.0$
$G_1/G_{0\infty} = 3.6$	$G_1/G_N = 0.78$
$G_2/G_{0\infty} = 2.3$	G_2/G_N 0.50
$G_3/G_{0\infty} = 0.94$	G_3/G_N 0.20
$G_4/G_{0\infty} = 0.42$	G_4/G_N 0.09
$G_5/G_{0\infty} = 0.2$	G_5/G_N 0.04
$G_6/G_{0\infty} \simeq 0.09$	G_6/G_N 0.02

4/22/65

Dan Pollen, Dieter Lux & Ajmone Marsan came to see me.
Pollen has concentrated on IPSP & conductance change in Betz cells — which have ≈ 10 meg Ω R_N
he finds for 8 to 10 mV IPSP a 40 to 60% conductance change

Lux has conc. on transient response to current pulse using $\log\{V_t \frac{dV}{dt}\}$ and get $\tau \approx 7$ to 10 mV pretty straight from $t \approx \tau$ to $t \approx 2\tau$

I told them that L as well as ρ can cause deviations & showed them my theoretical plots. I said I could probably dig out the slope fudge factor for a few values of L & ρ.

They have only a month or two left to finish their analysis.

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pursue pp 160-161 a little further to ask input conductance an electrode or a conductance change would see at different points, where $G_N = 6\,B_0\,G_{0\infty} = 4.6\,G_{0\infty}$

at $x = x_1$ $\quad G_1 = G_{0\infty}\left\{B_1 + \frac{C_0 + Z_0}{1 + C_0 Z_0}\right\} = (0.72 + 2.84)\,G_{0\infty} = 3.56\,G_{0\infty}$

or $\frac{1}{2}G_{0\infty}\{B_1 + C_1\} = G_{1\infty}(B_1 + C_1) = G_{0\infty}\left\{\frac{B_1}{2} + \frac{C_1}{2}\right\}$ ($G_{1\infty}$)

$= G_{0\infty}\left\{B_1 + \frac{C_0 + Z_0}{1 + C_0 Z_0}\right\}$

at $x = x_2$ $\quad G_2 = G_{2\infty}\{B_2 + C_2\} = G_{0\infty}\left(\frac{0.67 + 8.61}{4}\right) = 2.32\,G_{0\infty}$

at $x = x_3$ $\quad G_3 = G_{3\infty}\{B_3 + C_3\} = G_{0\infty}\left(\frac{0.54 + 7.02}{8}\right) = 0.94\,G_{0\infty}$

x_4 $\quad G_4$ $\quad \left(\frac{0.38 + 6.4}{16}\right) = 0.42\,G_{0\infty}$

x_5 $\quad G_5$ $\quad \left(\frac{0.2 + 6.0}{32}\right) \approx 0.2\,G_{0\infty}$

x_6 $\quad G_6 = G_{3\infty}(C_6) = G_{0\infty}\left(\frac{2.82}{32}\right) \approx 0.09\,G_{0\infty}$

Not returned to until 2/14/66; see p. 90 of Book 8

Finished I - Equivalent cylinder with closed ends

I-A Special case of constant $d\phi/dz$

~~I-B~~ Fig., limiting values, polarity comment, numerical

I-B Special case of exponential $d\phi/dz$

II - Equivalent Cylinder with Leaky Ends

II-A constant $d\phi/dz$

II-B exp. $d\phi/dz$.

Now need to write discussion of cases where different γ_0 & γ_m are needed, as for pyramidal cell, or even motoneuron with several dendrites one way & several another. Get, for example case that was used for Biophys. Congress.

Also, when two trees with different $d\phi/dz$ join at same soma, this can be handled by solving for $\gamma_{01} = -\gamma_{02}$ In other words, U_0 is such that the neg. slope of one matches the pos. slope of the other.

4/23/65 etc

Spent nearly all day writing draft of a paper entitled
Theory for Neuron Subjected to (External) Electric Field.
Succeeded in presenting all of Theory for sealed ends. Next to
do γ_0 & γ_m effect. ↳ also for $d\phi/dz$ = const & exp.

After writing, thought that axon case should be for $\gamma_0 = 1$, $\gamma_m = 1$

4/26 thru 4/29 Spent writing manuscript for ditto of above. Also, some
additional small calculations. Also wrote Gordon to bring
him up to date

4/29/65 Talked with Tom Reese & Milton about paper.
Tom raised several points to be analysed & discussed.
I - With regard to granule duration, consider { (a) fizzling active response
(b) sustained E transmitter action
II - Can we reject alternate inhib. pathways { (a) mitral axon collateral direct
(b) mitral axon collaterals to granule
III - Granule cell active or passive (do we need inhibition of deep end of cell
i.e. granule cell body & prox process?)
Tom feels evidence stronger for mitral sec to granule path, than for granule to mitral path.

I(a) & III failure to invade soma could be due to inhib. or to passive soma, or to long electrotonic
length (granule dendritic diam ≃ $\frac{1}{4}$ that of mitral ∴ for same materials, $\lambda \frac{1}{2}$)
(b) But could have sustained E & act like generator potential with occasional firing of cell
provided granule cells did not fire synchronously & did not invade dendritic periph
this would not prevent field.

II(a) would not explain field; would conflict with Dale principal, would require
prolonged transmitter action, & would not account for self limiting features
such as Yamamoto LOT does not add to IPSP produced by Commissure. Green et al
periodic antidromic following & blocking.
(b) also

Orrego, F. Arch. Ital. Biol. 1961, 99 446-465
1962, 100 1-16

Turtle bulb.
61 paper apparently suggests granule cell as inhib. interneuron

Hirata's title
Some observations on the fine structure of the synapses in the olfactory bulb of the mouse, with particular reference to the atypical synaptic configurations.
(Dept. of Anat., Sch. of Med., Niigata Univ., Niigata
Directors Prof. H. Koikegami and Prof. T. Yamamoto

The Reptilian Forebrain I – The Olfactory Pathways and Cortical areas in the Turtle. 425-445
II. Electrical Activity in the Olfactory Bulb. 446-465

Orrego p. 462 – sequence of events in mitral cell
p. 463 – granule cell excited by recurrent axons
includes idea of increased contrast i.e.
differential sensitivity to odours.
Also p. 464 – much spatial summation in glomeruli
to overcome depression following previous
synaptic activity in glomeruli.

Paper III in Vol. 100

p. 15 granule cells may have a tonic inhib. activity.

Orrego III – Cross Connections between the olfactory bulbs and the cortical areas in the turtle.

Orrego IV – pp 17-30 Electrical Activity in the turtle Cortex.

5/3/65 final push with Tom Reese & Milton Brightman to take account of literature.

Hirata, Yukio – Arch. histol. Jap. (Archivum histologicum japonicum) Vol 24, #3 (Feb 1964) pp 293–302 Title at left.

Andres – Zeitschrift für Zellforschung 65, 530–561 (#4 1965)

(Univ. of Kanazawa Med. Sch., Kanazawa, Ishikawaken, Japan)

Yamamoto, C, Yamamoto, T, & Iwama, K. (1963) J. Neurophysiol. 26, 403–415

Inhibitory Systems in the Olfactory Bulb Studied by Intracellular Recording.

rabbit

Place emphasis on $\boxed{\text{anterior commissure AC}}$ → interneurons → basal dendrites ||| secondary dendrites of mitral cells,

They quote Kerr & Hagbarth 1955 on and Orrego (1962) Arch Ital. Biol. on turtle.

Yamamoto work on rabbits.

p. 405 Intracellular spikes in presumed mitral cells 1.7 to 2.6 msec duration also could see IPSP following.

Used reversal depth of field potential as one method of identification. 0.8 to 1.2 msec latency.

This IPSP assoc. with inhib. & could be elicited with stim strengths below thresh. for axon of unit in question (my note, this is evidence for spread of effect, e.g. thru interneurons) They

* say it is presumably due to axon collaterals of neighboring mitral cells. (p. 406) ~~[illegible]~~ latency & time course of IPSP suggest interneurons to them (excited rhythmically by a single LOT shock

In deeper layers Yamamoto et al. found LOT shock set up single spike or spike train superimposed on prolonged depol. Latency of usually 3 msec or more. It is esp. clear that these spikes do not interfere with this epsp; they point to similarity to Renshaw cell.

Figs. 3-B & C show repet. firing in resp. to single LOT shock. Conclude that at least some of these deep cell firings participate in generation of recurrent inhib. They are counting these spikes, rather than the depol. as their sign.

Orthodromic (olfactory epithelium stim) also can produce mitral IPSP, but infer not monosynaptic pp 407-409 The deep layer cells do not ~~produce~~ show the IPSP.

p. 409 claim that AC repet. stim builds up IPSP much

* better than LOT repet. stim (this also fits well for our model)

p. 409-410 They are concerned that LOT antidromic does not

* add IPSP to that of AC stim; this is problem for them with collateral idea, but not for us, where mitral must fire to produce effect. Our model superior to theirs on these two counts.

p. 411 hard to locate inhibitory interneurons. should used extracell. recording So they are led to postulate two kinds of interneurons, shown as B_1 and B_2 in Fig. 100/p. 412

He has B_1 inhibit mitral cell & B_2 inhibit the LOT A interneurons

Thus he involves 3 kinds of interneurons, A, B_1, B_2

p. 413 Their A is similar to Orrego's granule cell

Yamamoto p. 413 point out the LOT does also have centrifugal fibers, which, Tom says, Green et al got rid of by degen.

We can agree with much of their discussion. However, they missed the possibility of mitral secondaries & thus focused on recurrent collaterals of mitral cells. This is the crucial difference.

Deep cells not stated to be granule, but some are claimed to to intermediates of IPSP generation. They have a slow depol. & sometimes rept. spikes. (But here we have to worry about centrifugal fibers!)

When orthodromic generates IPSP alone, we can assume that neighboring mitral cells did the job, via granule.

The Yamamoto story is slightly complicated by their finding the deep layer cells mostly inhibited by AC, but some activated. Their explanation is a possible one, but also problem of centrifugal fibers.

(rabbit)

Two papers by Green et al. in J. Neurophysiol. #4 July 1962

I Green, Mancia & von Baumgarten 467 — 488

II Baumgarten, Green & Mancia 489 — 500

Main title "Recurrent Inhibition in the Olfactory Bulb"

Subtitles I – Effects of Antidromic Stim. of Lat. Olf. Tract.

II – Effects of " " Commissural Fibers

Green Dal I — Antidromic LOT

p. 467 — { LOT contains mitral axons
Commissural fibers include tufted cell axons

p. 471 The periodic following & failing to follow at high frequencies could be due to accum. of long lasting J transmitter.

p. 474 Synaptically driven action potentials in ext. plex, did not follow well, had long latency, and were associated with second neg. peaks of evoked action pot.

bottom p. 474 — inhibitory pause after LOT (35 to 150 msec) present even when mitral cell in question did not fire

p. 476 They searched for a Renshaw type cell
Found no cells with such bursts.
Found a few spikes in ext. plex which they attribute to tufted cells

p. 477 nonseq. — they say that because mitral cells did not follow beyond 100/sec, the inhib effect did not require mitral cell body discharge. I don't agree; inhib could be prolonged result

p. 478 Fig. 8C is claimed to be a granule cell

pp 478 — 481 — reflected discharge back on axon

p. 484 Evidence for direct inhibition by axon collaterals.
(a) short latency
(b) at high frequencies, too high for interneurons to follow.
But our model does not require them to follow.
(c) massive nature, including also tufted & granule cells ?

(d) prolonged time of J which suggests accum of substance
rather than sustained Renshaw cell discharge.
(But we can have this too.)

Also, found no interneurons
& strychnine did not interfere

Rule out remote inhibition because OK
(1) this J blocks antidromic invasion
(2) whole spike, not just A spike (IS B) disappears.
They will discuss Dale's law in next paper.

X p. 485 lower ¶ They claim that the periodic following
is hard to explain with interneuron
which is stim by collateral — yes!

But this is precisely where our model comes to
rescue, because, when mitrals fail to fire, the
drive to interneuron also is cut off — but
of course, ~~they~~ the whole pop. won't be
synchronous? Their data suggests maybe it is?

485 upper ¶ — they think direct collateral better, but use
a weak argument that as SD spike unblocks, get reflex
discharge to double ~~the inhibition~~.

p. 486 they do mention Hartline & edge perception.

Baumgarten et al. paper II
Commissural Inpd.

Tufted cells provide output thru commissure to opposite bulb.
They assume that their A.C. stim is antidromic to tufted.

Found no antidromic invasion of tufted cells,
nor much if any orthodromic firing of granule cells.

Repet. stim of Commissure fibers CF produces inhib.
of cells of ext. plex., mitral & granule layers.

Important to bear in mind the Valverde result
about tufted cell axons not going non-stop
thru commissure. This explains why
tufted cells did not fire & spoils collateral
story of this paper!

p. 498 remarks on Dale Principal

Yamamoto & Iwama 1962 (Proc. Jap. Acad. 38
pp 63-67)
apparently then did not use interneuron

Phillips, Powell & Shepherd – J. Physiol 168, 65-88 (1963)

on p. 85 bottom, they argue that latency of (3 msec min) 3 to 50 msec suggests to them there must be at least one interneuron

p. 86 inhib. activity sometimes self limited as in Text fig. 7b

Shepherd p. 97, inhibition following single event last from 33 to 53 msec.

p. 99 cell recovers from refractory period before onset of the long lasting (11 msec) suppression of excitability; this is cited as evidence that this is not just a prolonged refractory period.

in case of weak olfactory nerve shock, get recovery at 4 msec & delayed unresponsiveness by 8 or 11 msec (p. 95)

p. 99 – Shepherd in 3rd paper will favor inhib by means of deeper lying neurons to mitral secondaries.

Shepherd – Neuronal Systems Controlling Mitral Cell Excitability.

Discharge of ~~[illegible]~~ other nerve cells within bulb

p. 105 latency: average = 3.8 msec after strong LOT shocks. 3-5 msec for mitral suppression

p. 106 some a little evidence of rhythmic suppression of mitrals.

p. 114 Distinguishes from Renshaw cell & suggests sustained transmitter action.

 5/4/65

Question - Shepherd p. 105 Fig. 3

shows (a) this mitral cell not invaded
(b) (c) & (d) it is invaded

My question - do I accept this interp, or is a change in the population response density? Can my theoretical model predict what should happen when nearest cell happens to fail? Not easily, because I assume uniform density leading to spherical equipotential contours. Then, I suppose I must superimpose minus an individual event. This implies an important theoretical problem to be solved for ~~grp~~ recording of group responses

5/5 & 5/6

1962
p. 323
Vol 137

Carrying on dialog with Tom Reese

He has been concerned about distinction between dendrites & axons. At my suggestion, he looked up Bodian's paper in Science (about 2 years ago) where Bodian points out the cell body is really not relevant to dendrite-axon distinction, he draws the jcn where the action potential arises. Tom has been much concerned about cytological criteria for dendrites as opposed to axons. My point is that Cajal called both granule & mitral dendrites, dendrites, though it is interesting that on pp. 661-662 Cajal thought that dendrites of internal granule cells, which articulate with dendrites of mitral cells, deliver excitation. & that in this sense, these dendrites would play the role of an axon cylinder, even though it does not have any of its attributes.

I suggested to Tom that dendrites are (1) what Cajal & others originally named as such, and (2) the functional resolution maybe that axons propagate impulses, but dendrites are devoted to synapses (now we allow both directions, where previously we thought only of receptive fcn) & the graded integration of synaptic effects. I pointed out that although I do not accept the Grundfest dogma, I am inclined to believe that all expts so far can be fitted with passive dendrites. Also, I convinced him that for small Z, passive dendritic depol. can be sufficiently spikelike to ~~be~~ seem adequate as a synaptic trigger (this point had worried him ~~&~~ he thought the presynaptic element would have to have an axonal action potential, and I persuaded him that this is not to be taken for granted). Given this point of view, he likes the idea of assuming all the mitral dendrites to be passive, & in this sense, non-axonal. (over)

This interests him also because he sees dendro-dendritic synapses in the glomeruli, where the mitral primary dendrite tufts appear sometimes presynaptic. My point is that, so far, I can explain all so-called evidence for dendritic impulse propogation as passive, but I have not disproved active — and, in particular, it is possible that there might be a low density of active patches which could provide ~~only~~ local response effects, rather than fast all-or-none spikes.

All this is relevant to the supposed anatomical basis for presynaptic inhibition, where, according to Tom, anatomists have simply assumed, when they see (A)→(B)→(C) that C must be a dendrite because it is postsynaptic, that B is i.e. an E ending and that A reduces the potency of B. However, according to our present model, B could be one dendrite and A & B could be portions of another dendrite.

Incidentally, in our model, there is a sense in which the mitral→granule could be called presynaptic excitation of the granule→mitral synapses, and there is also a sense in which the granule→mitral provides presynaptic inhib. of the mitral→granule synapses.

Tasks for writing (1) Sequence of events envisioned, and (2) ways in which this fits Green et al + Yamamoto better than than reflex collateral story.

5/7/65

Tom & Milton come over to talk some more

Tom also had roughed out some paragraphs where he felt that mitral secondaries can be regarded equally well as axon collaterals. But I demurred somewhat. How about dendrites being trees, as Cajal & others say & that we broaden our concept of dendritic fcn to include synaptic sending ~~as well as syna~~ and receiving as well as just synaptic receiving. In particular, we have mitral dendrites & granule dendrites as both presynaptic & postsynaptic in fcn. In some ways, all this seems simplest if there is no true action potential in dendritic membrane. Then one could agree with Bodian Science 137, p.323 (1962) at making the distinction at the point where impulses arise. Tom & Milton keep worrying about how to answer those anatomists who ask them to justify dendro-dendritic by justifying designation as dendrite rather than soma.

Just reread Bodian. I am reinforced in feeling that our point should be to generalize dendritic function further to permit synaptic sending. This deserve to be made explicit in a separate paragraph.

Kyoto

Ochi, J. Jap. J. Physiol. 13, 113–128 (1963)

Olfactory bulb response to antidromic olfactory tract stimulation in the rabbit.

R. von J. P. M.
Baumgarten, Green, Mancia EEG & Clin Neurophysiol. 14 621–634 (1962)

Slow waves in the olfactory bulb and their relation to unitary discharges.

Yamamoto & Iwama – Proc. Jap. Acad. 38 63–67 (1962)

IPSP is really an early prepublication of what is done more fully in J. Neurophysiol (1963)

K H Andres – Zeitschrift fur Zellforschung 65 530–561 (1965)

p. 558 2nd ¶
Opposite
~~Irrespective~~ of the postsynaptic structure (? web) in the granule processes, the synapses in the ext. plex layer are very similar to Gray's type II & .... may be presumed to be inhibitory. ... inhibitory & disinhibitory for
The feedback or control fcn could initially involve dendro-axonic (mitral-granule / granule-mitral) synapses, but more important would be the synapses on the granule perikarya & deep dendrites.

3/10/65

An important point in presentation of multiple working hypotheses, is not to emphasize that there is an answer to everything, but to emphasize that certain alternatives will be ruled out by certain observations. In other words, it is a way of stating present uncertainties, and of pointing to experiments which can rule out some of the possibilities. Thus, in case of granule & mitral cells, we must keep open both active & passive dendrite possibilities. Complete passivity of granule cell could be disproved ~~by~~ in principle, by recordings made from undeniable granule cells. Mitral secondary properties could be settled by intracell recordings near their periphery. etc.

Late in day, received letter from Gordon, with tracings, in which he says that period III is short and is followed by period IV, with reversed polarity. He guesses that period IV is either generated by the mitral cells while they are inhibited, or possibly granule cells ~~[illegible]~~ synaptic? presumably during some sort of recovery phase?

Re the 5/14/65 draft,

middle of page. Zvi thinks sentence starting, "Because" deserves more emphasis, such as italics or at least a new ¶,

I think a new ¶ would be good. Then also, one could add to end of preceding ¶ that only the granule cells can provide the necessary core conductance between the two regions.

5/10/65 — 5/14/65

This week we pushed thru a complete draft of proposed note to Science & sent off a Xerox copy to Gordon on 5/14/65. Still needs work on the references and probably some revision & possibly even amplification.

5/17/65 Let Phil Nelson read & spent day in library checking some of the references. Phil was not clear on whether the two kinds of inhibition would not produce current flows that would interfere with each other. Necessary to point out why the granule current & voltage would be sig. greater than the mitral. Also, may need footnote to state that assertions are based upon a computational simulation. The presynaptic inhibition implication did not get across. May want to emphasize granule cell core conductance thru mitral body layer; Tom says this is very impressive in some of their pictures. Also, probably should more explicitly relate high frequency of golgi spines with high freq. of the small things we are calling gemmules in the e.m. The periodic firing & non-firing must be more clearly distinguished from alternation, which Phil regards as explainable by refractory period.

In library, found Ochi paper interesting.

I must soon write up the points contrasting single neuron & pop. of synch & asynch neurons. This slanted dipole of F.R. —>, if it means anything, could mean an asynchronous sequence along a layer.

To test such ideas & also effect of number of cells, need to compute values along a grid of parallel axes, to permit superpositions.

Axes

First, superpose different numbers of synchronous elements at same depth.

Then, vary (a) depths
(b) synchrony (i.e. staggered timing)

5/20/65

Talked with Karl Frank - briefly about Fred Rosenthal's single dipole model and then about our manuscript, interesting, but not a basic model (What about other side of dipole? Phil suggested that slanted dipole really means a conically arranged set, but then get different field. Also, used the formula for $r >> l$, $\therefore$ excluded wide spacing. It is time that I publish the large & small scale pictures done with Jeanne & Ezra.

K.F. & Phil comments

K likes idea of passive dendritic role & Phil pointed out that graded effect is consistent with NM jcn work.

Castillo & Katz (1954) 124, 586-604

Liley 1956 134, 427-443 & maybe later.

K pointed out that periodic firing & non-firing could be by means of afferent to ordinary J. We cannot easily exclude this, except possibly in terms of probabilities

Also, he noted that even when antidromic blocks in one neuron, J could get thru by neighbors if they don't block, which is true; however, I am assuming that pop. is working together under these conditions. Needs to be clearer.

They think recurrent inhibition means via recurrent collateral. Phil suggested autogenetic. How about self as well as lateral inhibition.

5/21/65

Tom brought over his friend, Forrest Waight, who had several questions. In particular, he ~~I~~ realized that I was not consistent with field around single neuron & wondered how come. Apparently this is going to force the issue about how I calculate the field potential. I begin to think that I better write up a short note on this too. I told him a little about it, that there would be concentric isopotential contours, that the potential would be const. at center if there were no sources at smaller radius.

I_e = current density in cylinder

$$V(x_1) - V(0) = -\int_0^{x_1} I_e R_e \, dx$$

* Method of computation is to use soma dendritic model to compute I_i & then, from this compute V_e, relative to some specific reference point.

5/24/65 – 6/4/65 –

Received Gordon's comments & suggested revisions –
also spent a little time with the literature
Finally 6/1/65 – 6/3/65 ground out a fourth draft, Tom revising
the anatomical part & I patched together & revised
the pieces of the physiological presentation.
Today we aim at a final typing for Neuroanat clearance & to
send to Gordon on Monday after he phones us from Cold Spring
Harbor.

This version was cleared

6/8/65 send to Gordon c/o Gergely at Retina Foundation
Also T.R. – Gordon on telephone expects to be here ~ 6/16

Gordon induced Tom & Milton to revise and proof
6/15/65 – 6/18/65 revised manuscript with all authors present.
on 6/18 Tom & I tried to incorporate Gordon's comments on physiol & anat part
6/22/65 final push to completion of final version.

6/23/65 Now Gordon & I have until about 6/30/65 to work
on main paper & figures & slides

~~WXR~~

WXR 795C
WXR 93C
94C
95C
82C

Run successfully 6/16/65

This shows that passive membrane with E in dendrites will work. However, because granule cells deeper than mitral, change ~~SHCF~~ PDF to 0.5 from 0.25 The fall off of the EPL Negativity, radially outward, could be due to SHCF which might be larger than for mitral cell. In view of this, consider letting E be flat in the dendrites. , try in new problem .8222

.8224

However, possible that mitral cell effect would decrease with distance

6/14/65

Decided to try a fresh Granule cell run for passive case, But also to rerun slight mod. of last weakly active Granule run.

Previous Granule runs were

64795.8215 } 9/15/64 see page 84 of book 4
.8216 }

.8217 } 10/6/64 see page 34 of book 5
.8218 }

These used very cool kinetics & also substantial inhibition to prevent ~~spread~~ invasion of axonal end.

Set up 65795.8219 as very slight mod. of .8218

Here reduce NT to 51 from 70
RHOSOM to 0.8 from 1.0

<=> 65795.8220 IFAB = +1 passive dendrites.

see next page .8222 8224

RACT = RBSQ = RBFR = .001
effectively passive soma & axon

Also UA = UD = USA = USD = 50. instead of 25
because this makes ΔZ = .14
which is ample for 12 compartments

also, changed DT to .02, NEJ = 4
and changed BEB cards.

65795.8222 6/17/65 flat E in outer 6

65795.8224 6/24/65 decreasing E in outer 6 to simulate synaptic stim from mitral secs.

All of these worked quite well.

used flat case for Fig. 10 of draft for paper

6/15/65 Gordon arrived Tuesday morning.
Discussed with him & Tom in morning. Afternoon tied up with Karl Frank contract with APL discussion

finished Science draft with Gordon & Tom on 6/22/65

Worked with Gordon on figs. & draft for the main paper over 6/23/65 thru 7/1/65

7/2/65
Now must take figures to art department, and make sure of having slides ready for the trip to Tokyo. Also must ~~take~~ care of Tokyo reservations etc.

Also, in Gordon's ~~single~~ muscle spindle work with David Ottoson, they obtained relations between frequency of firing & stretch — esp. linearly increasing stretch. Also, with an anaesthetic observed generator potential. Recordings were from nerve fiber in oil, versus ref electrode in the bath.

This reminds me also to remember problem of recording condition I had at dorsal roots in thesis problem. Could explore these theoretically sometime.

6

Let the equivalent cylinder extend
from $Z=0$ to $Z=Z_m$.

while for steady synaptic conductance
changes

$$I_m R_m = \lambda^2 (V - V^*)$$

in the notation of (Rall, 1962a).

1a

Fig. 1A

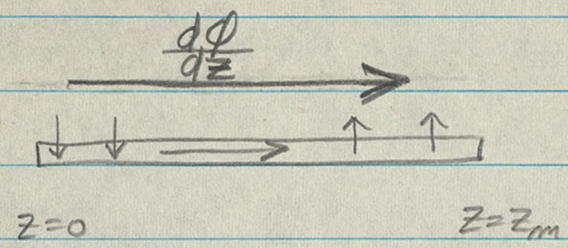
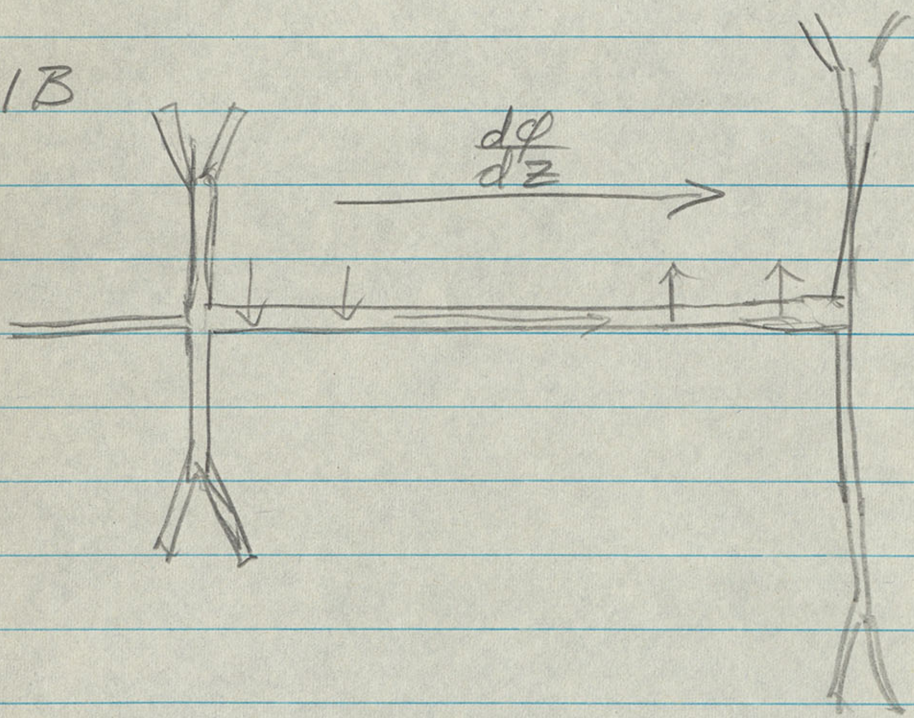
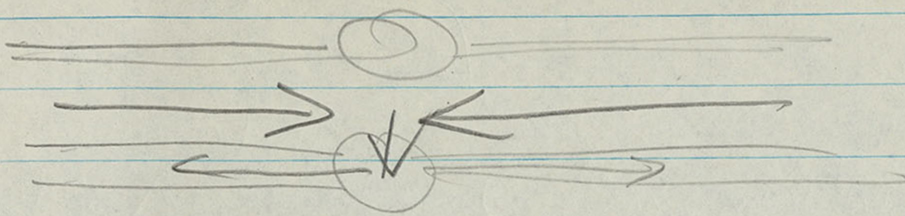
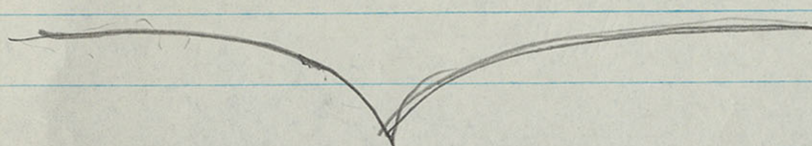


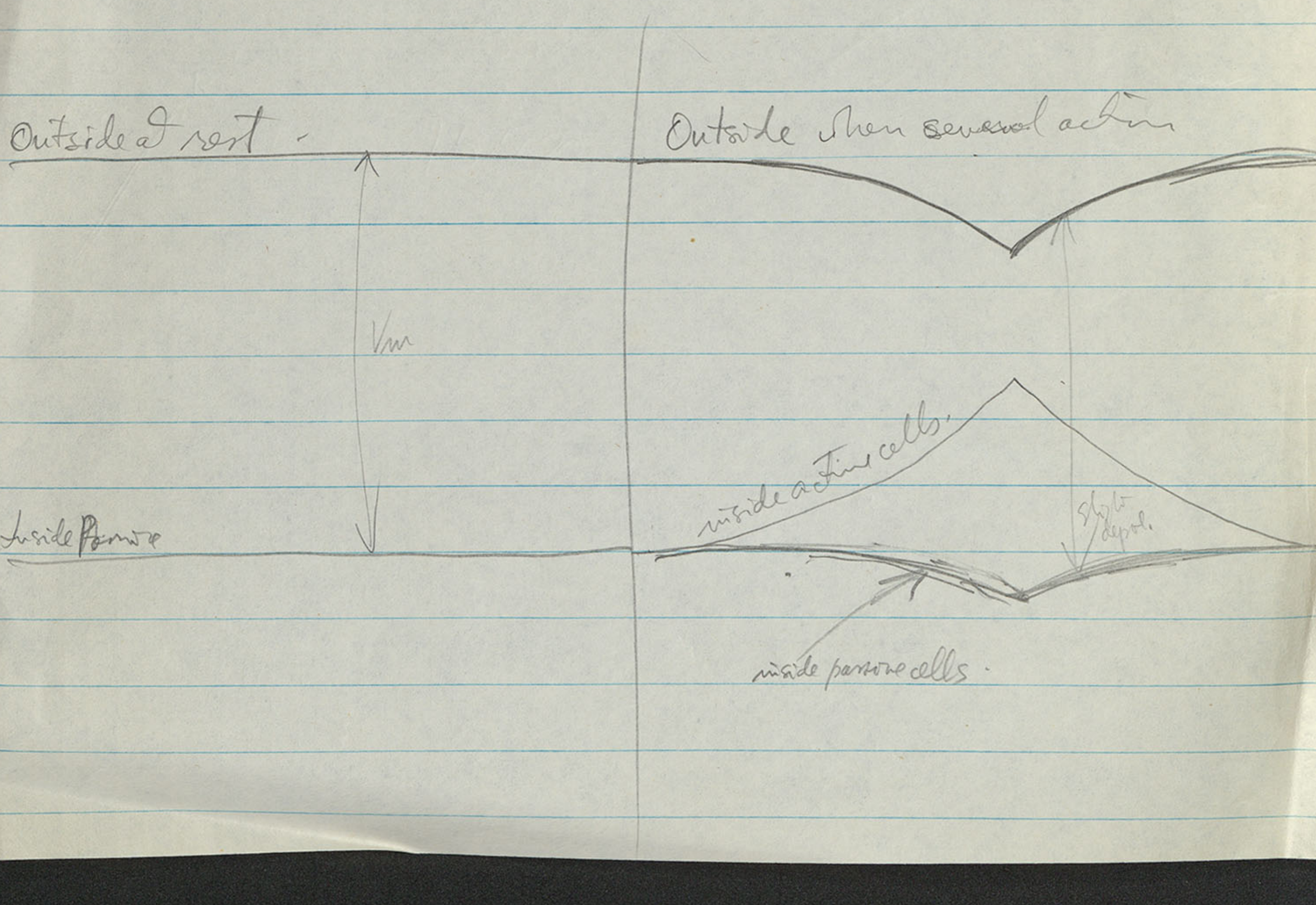
Fig. 1B



When a neuron is subjected to a ~~applied~~ gradient of extracellular potential, how can one calculate the magnitude and distribution of the resulting membrane depolarization and hyperpolarization? Given a theoretical basis for such calculations, ~~are do~~ are the magnitudes of these effects sufficient to account for significant changes in neuronal firing probabilities and firing frequencies?







Outside at rest -
Outside when several active
Vm
inside active cells.
slight depol.
Inside passive
inside passive cells.

June 10, 1965

Memo regarding manuscript entitled "Interaction between spinal motoneurons of the cat."

Dear Phil,

This is very interesting. As I said on the phone, my principal comments concern the interpretation of Fig. 2.

On first reading, I accepted the argument on pages 7 and 8 (regarding Fig. 2), but, on reconsideration, I do not. Figure 2 does not show that "firing occurs at a lower level of depolarization than ... with the unconditioned response". The extracellular antidromic field potential (neg. peak) is presumably of larger magnitude than the intracellularly recorded neg. peak. In other words, your word "depolarization", as you have used it, is not the same as "membrane depolarization".

My interpretation would be that the soma interior would not simply ride with the extracellular potential, because the soma interior is electrotonically tied to the dendritic interior. Thus, if the soma exterior has a larger neg. dip than does the soma interior, the net result is soma membrane depolarization, whereas, if the soma interior actually rode with the soma exterior, this would imply no net soma membrane depolarization. It would be interesting to compare actual extracellular and intracellular neg. peaks for the same antidromic valley.

In view of this, it does not seem necessary to assume greater membrane depolarization at the trigger zone. This seems safer to me, because it might require rather special geometric relations between active and passive cells to insure preferential depolarization of the axon hilloc.

The Journal of Neuroscience

The official journal of the Society for Neuroscience

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1/29/65

Bill Hogin's point is in effect that a good theoretician ought to be able to design some crucial experiments; (otherwise he may be dealing only with pseudoproblems.

This is certainly the position of Hodgkin + Katz, et al. & does have impact on the field — a good experiment, carefully interpreted, is irrefutable.

However, it does not necessarily follow that somewhat more abstracted problems are not important. Think of Gibbs & theoretical physicists.

Bill suggests That key problems are

synaptic transfer function

and - good exp. measurement of λ and τ

Ted Lewis wanted examples of predictions that were confirmed. Actually my 1957 paper made predictions that were confirmed.

Also Extracellular Potential.

Also soma equalization time const.

Also 1956 with Hunt.

Also, inhibition at soma (Rall 1960 IPSP
Rall 1961-2

11/21/67

Memo regarding contrast in summation of dipolar and multipolar components of neuronal fields.

Theoretical aspects and conjectured demonstration in case of spinal cord antidromic activation.

These notes recap. old notebook notes from Feb + March 1965, just before dendro-dendritic EM results became known to me. (pp 25-31, 40-41, 44-49, 83 Book 6)

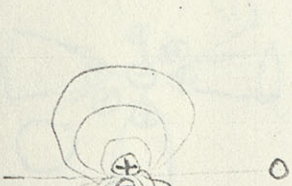
Zero order multipole = point charge q, say at $z = +l$

$$\varphi(r,\theta) = \frac{q}{4\pi\varepsilon}\left\{\frac{1}{r}\sum_{n=0}^{\infty} P_n\left(\frac{l}{r}\right)^n\right\}, \quad \text{for } r > l$$

$$= \frac{q}{4\pi\varepsilon}\left\{\frac{P_0}{r} + \frac{P_1}{r}\left(\frac{l}{r}\right) + \frac{P_2}{r}\left(\frac{l}{r}\right)^2 + \cdots\right\}$$

for $r \gg l$, $\frac{P_0}{r}$ dominates

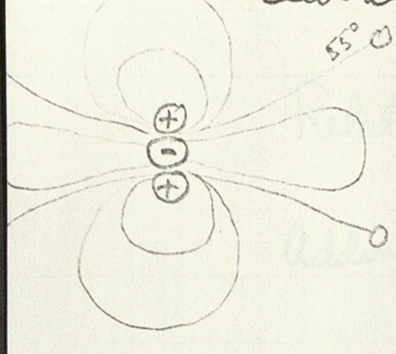
First order multipole = dipole : $+q$ at $+l$, $-q$ at 0



$$\varphi(r,\theta) = \frac{ql}{4\pi\varepsilon}\left\{\frac{P_1}{r^2} + \frac{P_2}{r^2}\left(\frac{l}{r}\right) + \frac{P_3}{r^3}\left(\frac{l}{r}\right)^2 + \cdots\right.$$

for $r \gg l$, $\frac{P_1}{r^2}$ dominates

Second order multipole = quadrupole

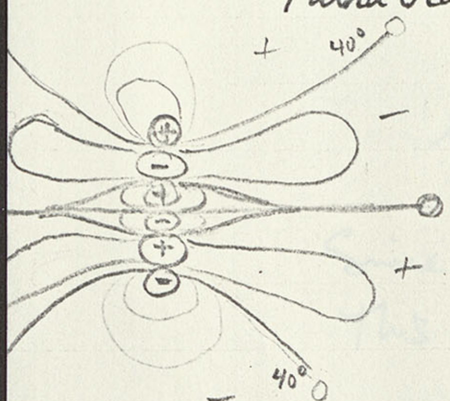


Axial quadrupole: $+q$ at $+l$, $-2q$ at 0, $+q$ at $-l$

$$\varphi(r,\theta) = \frac{2ql^2}{4\pi\epsilon}\left\{\frac{P_2}{r^3} + \frac{P_4}{r^3}\left(\frac{l}{r}\right)^2 + \cdots\right\}$$

(Note: P_3 drops out because of symmetry)

Third order multipoles = octapoles $\quad \frac{12ql^3}{4\pi\epsilon}\frac{P_3}{r^4}$ leading term



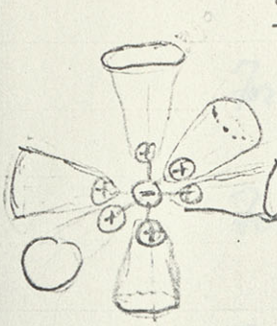
Axial octapole $\quad$ ⊖—(2+)—⊖ $\quad$ ⊕—(2−)—⊕

parallel $\quad$ ⊖—(2+)—⊖ / ⊕—(2−)—⊕ $\quad$ } Conjectured

Also $\quad$ ⊕/⊖ ⊖/⊕ ⊕/⊖ ⊖/⊕

or parallel plane arrangement

Fourth order multipole = dodecapole ?



Three orthogonal quadrupoles of equal strength

~~Relative~~ ~~of ... axial factor~~ $\quad \varphi(r,\theta,\phi) = \frac{2ql^4}{4\pi\epsilon}\left\{\frac{P_4(\gamma_1)+P_4(\gamma_2)+P_4(\gamma_3)}{r^5} + \cdots\right\}$

where $\gamma_1, \gamma_2, \gamma_3$ are the direction cosines of the field point relative to the three axes.

(Note: P_2 drops out because of symmetry)

See next page

$$P_2 = \frac{1}{2}(3\cos^2\theta - 1)$$

Relative to each octapole axis, have $\cos\theta$ as $\gamma_1, \gamma_2, \gamma_3$

Adding the three contributions ~~of~~ $\frac{P_2}{r^3}$, obtain

$$\sum \frac{P_2}{r^3} = \left(\frac{1}{r^3}\right)\left(\frac{1}{2}\right)\left(3\gamma_1^2 - 1 + 3\gamma_2^2 - 1 + 3\gamma_3^2 - 1\right)$$

$$= \left(\frac{1}{2r^3}\right)\left\{3(\gamma_1^2 + \gamma_2^2 + \gamma_3^2) - 3\right\}$$

$$= 0$$

because $\gamma_1^2 + \gamma_2^2 + \gamma_3^2 = 1$

Since P_3 term was already missing from quadrupole, this leaves P_4 as lowest order term.

Now $P_4 = \frac{1}{8}(35\cos^4\theta - 30\cos^2\theta + 3)$

$$\sum P_4 = \frac{1}{8}\left[35(\gamma_1^4 + \gamma_2^4 + \gamma_3^4) - 30(1) + 9\right]$$

For $\gamma_1 = 1$, $\gamma_2 = 0 = \gamma_3$, get $\frac{35-21}{8} = \frac{14}{8} = 1.75$

For $\gamma_1 = \gamma_2 = \frac{\sqrt{2}}{2}$, $\gamma_3 = 0$, get $\frac{35(2\cdot\frac{4}{16}) - 21}{8} = \frac{17.5-21}{8} = \frac{-3.5}{8} = -.44$

For $\gamma_1 = \gamma_2 = \gamma_3 = \sqrt{.333}$, get $\frac{35(3/9) - 21}{8} = \frac{11.67-21}{8} = \frac{-9.33}{8} = -1.17$

Important to remember that when $r \approx l$, one must use the expression

$$\varphi(r,\theta) = \frac{q}{4\pi\epsilon}\,\frac{1}{\sqrt{r^2+l^2-2rl\cos\theta}}$$

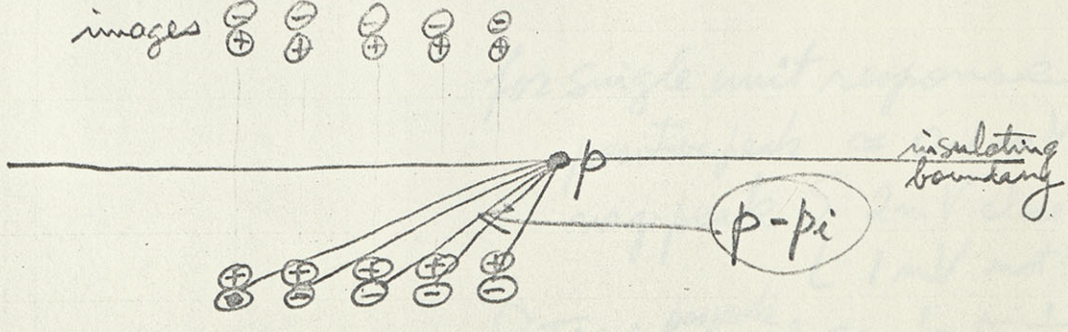
for each pole, esp. for θ small.

Also, if wish to consider an insulating boundary at finite distance, can use method of images. In particular, if consider only one such plane boundary, the potential at the boundary will be exactly **twice** that which would be obtained for infinite extent. If a curved boundary, need to consider unequal images or chains of images.

For summation of several units, need to know

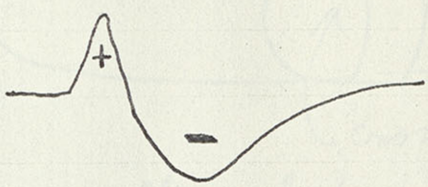
(a) spacing of units in planar array
(b) how many planes
e.g. (c) number of units, either explicit or implicit
(d) orientation of units

Then $\Phi(p) = \sum_i \varphi_i(p-p_i)$



Most general problem would permit
(i) variable orientation of units
(ii) variable spacing " "
(iii) variable weighting of P_1, P_2, P_3, P_4
(iv) variable strength of units
(v) temporal dispersion of activity
(vi) different frequency components
(vii) complicated boundary conditions

Consider now, antidromic activation of synergic group of motoneurons in lumbar region of cat spinal cord.



for group response (Van Buren)
positive peak 0.4 to 0.8 mV
neg peak 1.5 to 3.7 mV

$$\text{Ratio of } \frac{\text{pos. peak}}{\text{neg peak}} \simeq \frac{1}{5} \text{ to } \frac{1}{3}$$

---

for single unit response
positive peak $\simeq$ 0.1 mV
neg peak $\begin{cases} \text{2 mV close to soma} \\ \text{1 mV not so close} \end{cases}$

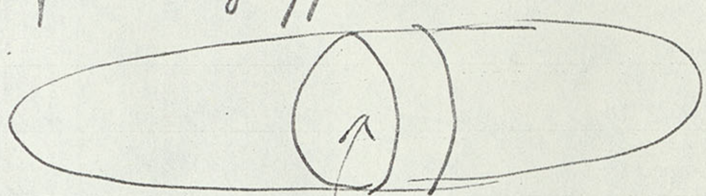
$$\text{Ratio of } \frac{\text{pos peak}}{\text{neg peak}} \simeq \frac{1}{20} \text{ to } \frac{1}{10}$$

∴ group neg. attributable mainly to 2 to 4 nearest neighbors
" pos. " 4 to 10 [illegible] small contrib.

Here is a crude numerical interpretation that I put on page 48 of old notebook.

	pos. peak	neg. peak
nearest unit	0.1 mV	1.2 mV
four next nearest (~140μ)	0.2	0.8
" " (~200μ)	0.1	0.4
8 " (~300μ)	0.1	0.1
16 " (~400μ)	0.1	0
	0.6 mV	2.5 mV

Van Buren found gastrocnemius nucleus to have following approx dimensions 9.9 mm long
.8 mm dorsoventral
.6 mm lateral

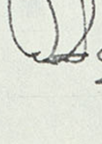


cross-section ≈ .48 ≈ .5 mm^2

ellipsoid of revolution has volume approx 2.5 mm^3

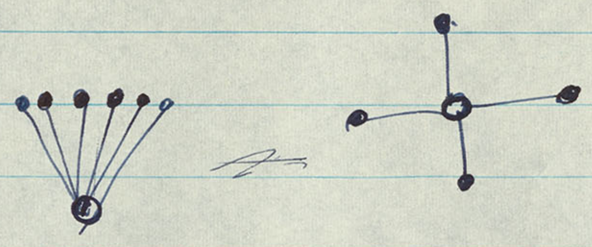
Number of units (large motoneurons) stated ≈ 370
chromatolised.

He said chromatolysis density ≈ 160 per mm^3 at L_7
also ≈ 180μ between cells
plus 630 per mm^3 belonging to other muscles



Slab 100μ thick has volume ≈ .05 mm^3 contains ≈ 8 units
200μ " .1 16

Dendritic current complicates story, but maybe can make the point



add ~~four~~ six dipoles this way

Then add six dipoles this way

Then compare spatial decrement even along axis

well away from dipole we have $V(r) \propto \frac{1}{r^2}$ i.e. $\frac{P_1}{r^2}$

p. 175 $\frac{\vec{p}\cdot\vec{r}_0}{r^2}$

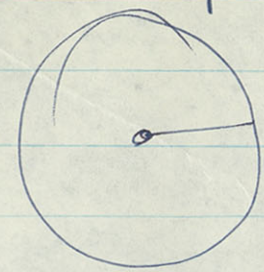
or $\vec{p}\cdot\nabla\left(\frac{1}{r}\right)$

Stratton p. 181 multipole $\phi_n \propto \frac{Y_n}{r^{n+1}}$

where n is the number of dipoles in different directions.

where Y_n is a fn of cosines of angles between $\vec{r}$ ~~and~~ the n axes and the direction cosines of these axes.

Spherical or multipole field



curve F of fig. 10 in 1962 Biophys. J.

assuming linear I_e falling to zero at $R=B$

$$V_e \cancel{\propto} \left[\frac{(B/R) - 1 - \ln(B/R)}{B-1}\right]\left(-\frac{I_s R_e}{4\pi b}\right) \qquad R = \frac{r}{b}$$

$$\text{or } V_e(r) \propto \left[\frac{bB}{r} - 1 - \ln(bB) + \ln r\right]$$

Note: $\dfrac{dV_e}{dr} \propto \dfrac{c-r}{r^2}$

where we are not too concerned about values as $r \to C$

2/3/65 Phil Nelson called
~~comparison~~ of unit data with population data

Van Buren

Bob Burke with Phil

pos. .1
neg. 1

factor of 10

~~$~~ 6/10 Van Buren

Phil
factor of 20

$\frac{neg}{pos} \approx \frac{2\,mV}{100\,\mu V}$

Also, Van Buren ~~[illegible]~~
can see unit contributions to the negativity, but presumably not to the positivity.

~~Mon~~ 7/9

Tues lunch with Phil Nelson
confirm on Monday

...UM OF CALL

Date	Time

☐ YOU WERE CALLED BY— ☐ YOU WERE VISITED BY—

TELEPHONE:	Number or code	Extension

☐ PLEASE CALL
☐ WILL CALL AGAIN
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☐ IS REFERRED TO YOU BY:

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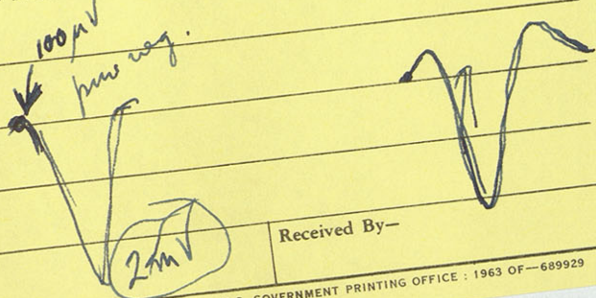
☐ WISHES AN APPOINTMENT

Phil.

LEFT THIS MESSAGE: Half of these



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63–106

NO. 340-M DIETZGEN GRAPH PAPER
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from Phil Nelson
3/2/65

CAT 1557

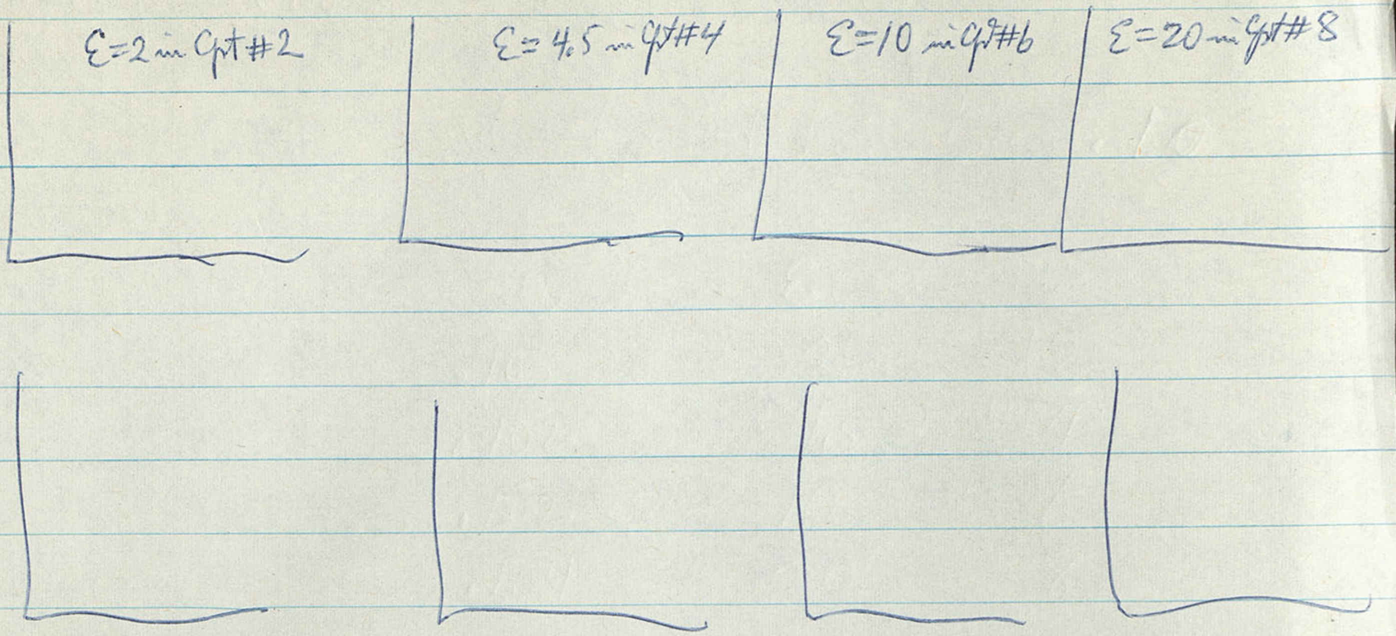
— in ventral horn in region of motoneurones

— Deep in ventral root region.

P. G. Nelson

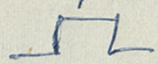
Compare $\varepsilon = 2$ in compartment #2

with $\varepsilon = 20$ in compartment #8 which is 1.2λ farther out



ε=2 in Gpt#2
ε=4.5 in Gpt#4
ε=10 in Gpt#6
ε=20 in Gpt#8

step size = .05 T

 5ΔT = .25 T

Referring back to pp 89 ~ 115 of Book 6

Perhaps should add perturbations to cpt. 10

But we have already peak in ① for ε in this

.103	2	in cpt 2
.102	4.5	4
.102	10	6
.104	20	8

est. 0.014	3	in cpt 2
"	6.5	in cpt 4
0.16	20	in cpt 6
0.143	40	in cpt 8

0.19	ε=4	in ②
.192	10	④
	try 30	in ⑥
	try 60	in ⑧

Should do run with E_ϵ & E_j connected in & with appropriate summer — see p. 95

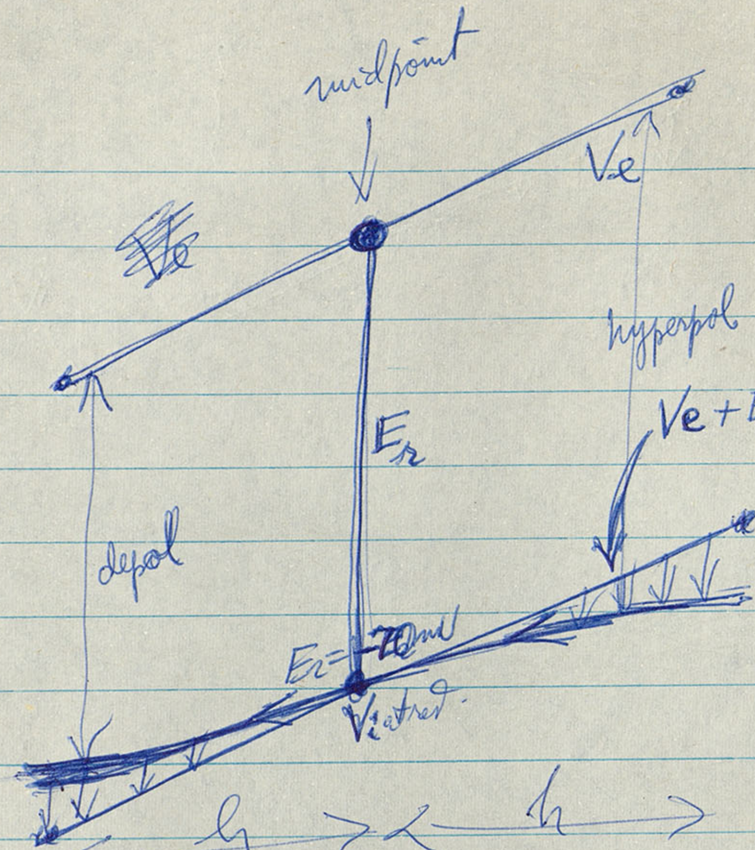
Compare $\varepsilon = 2$ + $\varepsilon = 4$ at Cap 2

$\varepsilon = 2$

$$\frac{\text{slope at half peak}}{\text{peak}} = \frac{.0705 - .023}{(0.1)(.103)} \simeq 4.7$$

$\varepsilon = 4$

$$\frac{.1335 - .0448}{(0.1)(.19035)} \simeq \frac{0.98}{.2} \simeq 4.9$$



let h = halflength

$$\frac{dV_e}{dx} = c, \quad \frac{dV_e}{dZ} = b = \lambda c$$

Now $V = V_i - V_e - E_r = \lambda c \left\{ \frac{\sinh(\frac{1}{2} L/\lambda - x/\lambda)}{\cosh(\frac{1}{2} L/\lambda)} \right.$

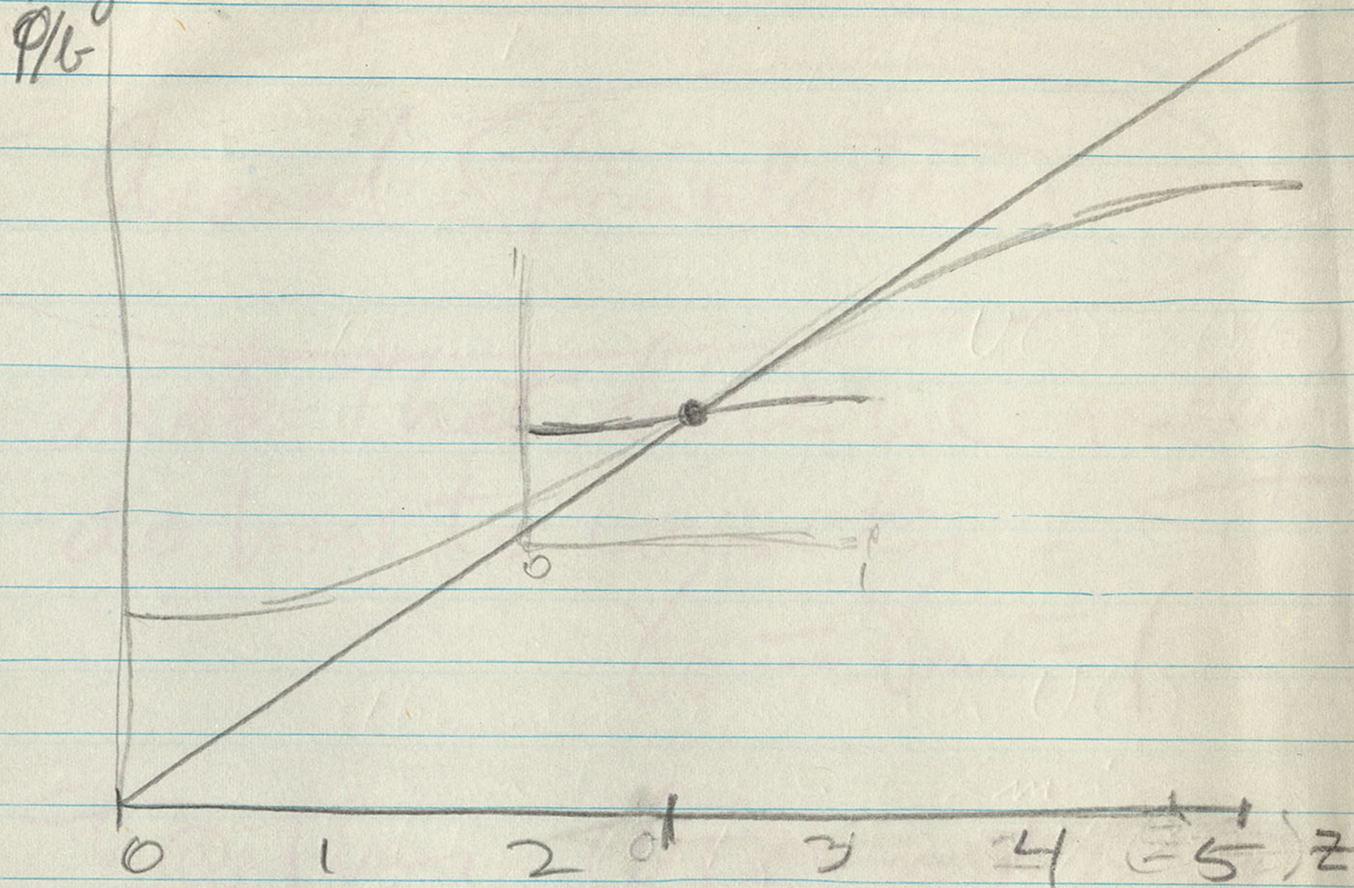
and $V_0 = \lambda c \tanh(\frac{1}{2} L/\lambda)$

$= \lambda c \tanh(h/\lambda)$

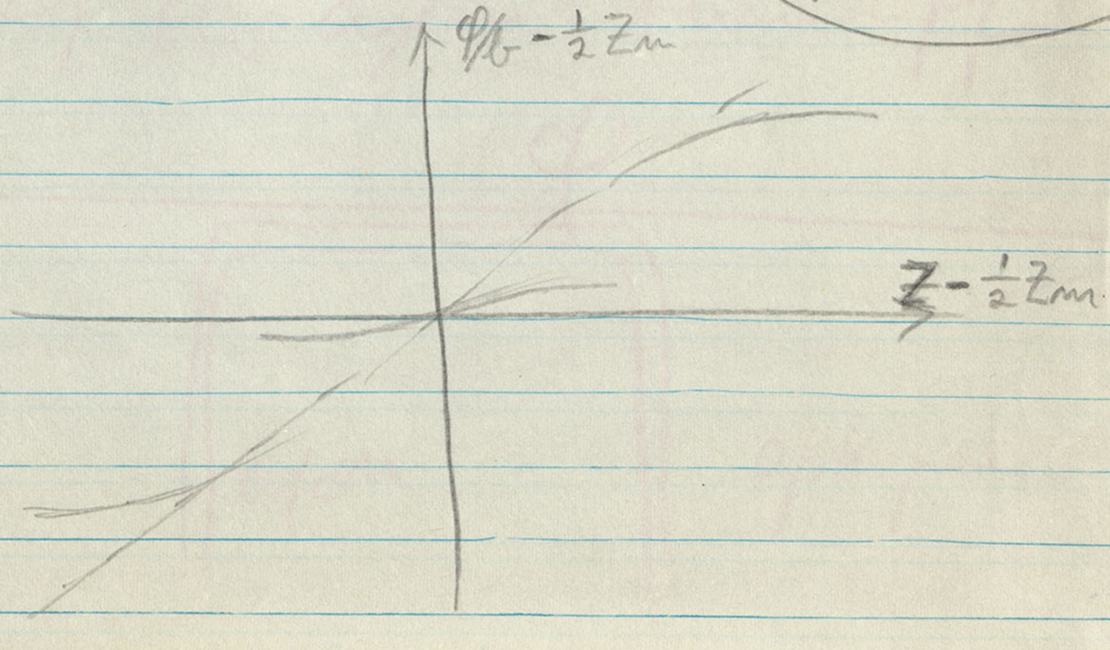
for $h/\lambda < 0.2$, get $V_0 = hc$

for $h/\lambda > 2.3$, get $V_0 = \lambda c$

Fig. 1



If both centered, can show as $\varphi/b - \frac{1}{2} Z_m$



4/28/65

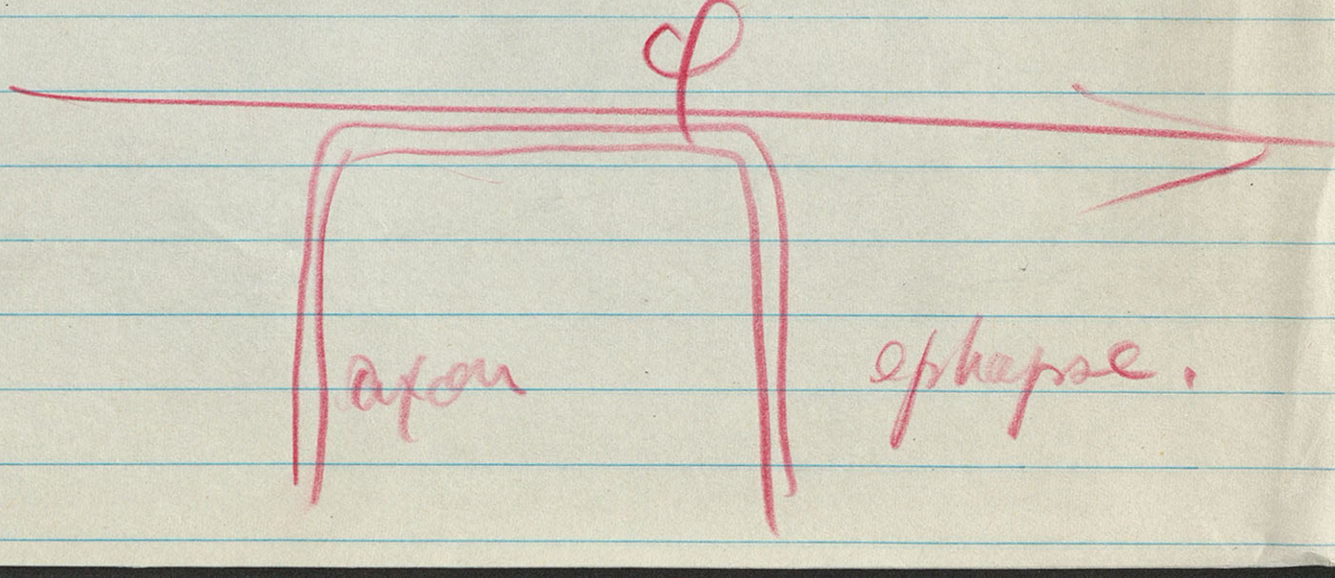
Axonal Stimulation

note that here we really do have to consider

$$\gamma_0 = \gamma_m = 1$$

& either $\phi(z)$ is of finite length

or the axons turn off



~~also $\frac{dU}{dx}$ a~~

at $Z = \frac{1}{2} Z_m$

$$\frac{dV}{dZ} = \frac{-b}{\cosh(\frac{1}{2} Z_m)}$$

$$\therefore \frac{dU}{dx} = b\left(1 - \frac{1}{\cosh(\frac{1}{2} Z_m)}\right)$$

Superseded

Then we can write

$$V_0 = \lambda c \tanh\left(\frac{X_m}{2\lambda}\right) \qquad (23)$$

which has relevance for relative stimulus thresholds of axons which differ only in diameter. ~~subjected to a constant current [illegible] a distant [illegible] flowing longitudinally.~~

If long lengths of such axons are subjected to a constant external gradient, the magnitude of membrane depolarization near the cathode and should be proportional to λ and hence to the square root of diameter. For long lengths, the hyperbolic tangent has a value of 1.0, and one should expect the critical stimulating gradient to be inversely proportional to λ or to $\sqrt{d}$.

4/23/65

Introduction — Simply say that will consider specific examples of $\frac{df}{dZ}$ const & exp. function of Z.

Present closed & γ_0 & γ_m cases before going into

Also, note that $\gamma_0 = 1$, $\gamma_m = 1$ is the best approx to the case of axons $\therefore$ should ~~use this~~ case in applications to ~~axons~~

2nd ¶ of introduction — ~~Many of these~~ ~~Many of~~

Most of these theoretical results were obtained in 1961 ~~and~~ ~~the results of calculations were included~~ in a paper presented at the first Intl Biophysics Congress (Stockholm 1961) see Rall, 1962b)

18a

Compare with

axons, $\gamma_0 = 1$, $\gamma_m = 1$, $\frac{d\mathcal{L}}{dZ} = \lambda C$

Then

$$U_0 = \frac{b}{2}\tanh\left(\frac{X_m}{2\lambda}\right)\left\{\frac{1+\coth\left(\frac{X_m}{2\lambda}\right)}{1+\coth\left(\frac{X_m}{\lambda}\right)}\right\}$$

for X_m very large, $\coth = 1$

and get $U_0 = \frac{\lambda C}{2}$

If very short get $\frac{b}{2}\left(\frac{X_m}{2\lambda}\right)\left(\frac{1+\frac{2\lambda}{X_m}}{1+\frac{\lambda}{X_m}}\right)$

$$\frac{X_m+2\lambda}{X_m+\lambda} = 2 - \frac{X_m}{\lambda + X_m}$$

& $\gamma_m = 1$

whereas if $\gamma_0 = 0$, then

$$U_0 = b\tanh\left(\frac{1}{2}\cancel{\frac{X_m}{2\lambda}}\right)\left\{\frac{1+\coth\left(\frac{1}{2}Z_m\right)}{1+\coth Z_m}\right\}$$

alternatively get $b\left(\frac{e^Z-1}{e^Z}\right)$ for $\gamma_0 = 0$, $\gamma_m = 1$
whereas $\gamma_0 = 1$
gives 2 in denom

$= b(1-e^{-Z})$

for Z very large, get b, for Z very small, get bZ

18b

Suppose $\gamma_0 = -1$

$\gamma_m = -1$

Then

157a

Tom Reese and Milton Brightman are attending a ~~[illegible]~~ meeting of anatomists in Miami this week. They ~~will have~~ will display a demonstration consisting of many of their pictures at various levels of the bulb, and will include their most recent findings together with something of our interpretation. They feel that it will be urged to get ~~our note out of~~ to work on the joint note as soon as they return. I prepared the enclosed memo, because

I saw a preview of their display on Friday, April ~~[illegible]~~ 16. It seems that they have done additional searching of external plexiform layer since the time Tom ~~they~~ talked with me, and they now have many examples of ~~Type I~~ typical looking type I synapses directed from what must be mitral secondary dendrites to what ~~are presum~~ appear to be gemmules, presumably of granule cell dendrites, and also many examples of type II synapses directed the other way, and

Zeitschrift p. 172 c

K. H. Andres
p. 558 2nd ¶

Apart from the unusual contrast of the post. synaptic ~~membranozone~~ (web) in the processes of granule cells, ~~and~~ they similar to ~~the~~ the synapses ~~of the plexiform layer~~ of Gray's type II.

The synapses in the ext. plex layer are

Apart from web, he ~~says~~ that the synapses in ext pl layer resemble Type II & may be presumed to be inhibitory.

∴ synapses in ext plex mediate ~~assumed~~ inhibitory & disinhibitory effect upon mitral & tufted cells!

The control function could initially involve dendro-dendritic synapses (granule mitral) but more important would be the synapses on the granule perikarya & deep dendrites.

p.1726

Kyoto

Ochi, J.

Japanese J. of Physiol. 13
113 – 128
(1963)

Olfactory Bulb Response to Antidromic Olfactory Tract Stimulation in the Rabbit.

Fig. 2 on p. 116 is interesting

Compares orthodromic LOT AC versus depth.

AC shows only a deep neg

5/3/65

Green papers ① They reject interneuron, because they think only of Renshaw cells & cannot find them.

② They did not think of prolonged I from interneuron

③ They did not think of mitral secs, which provide for an explanation of their periodic phenom — which they beg.
But infact, could do very well

? They get inhib even when mitral cell does not fire.
My question is, how far away could nearest firing mitral cell be without their seeing it.

Yamamoto

They use granule cell as interneuron, but use ~~ret~~ collaterals to stim them.

This causes them trouble with AC — LOT interactions, which we can get around.

Also, they postulate 3 kinds of interneurons A, B_1, B_2

Their deep cells fire rep. — but not definitely granule.

Points that trouble Yamamoto, but not us.

(1) Repet. LOT is much less effective than ~~f~~ repet AC in building IPSP initial

They have trouble, because their reflex collaterals should get them to interneuron, whereas, when inhibited, our secondaries would not.

(2) Similarly, for failure of LOT to add to IPSP already made by AC.

1292

Several people agree that ¶ at bottom of page 7 & top of p. 8 needs revision.

Zion wondered about "previously"

I notice the emphasis on granule.

But actually, both sets of dendrites both send & receive.

Bodian / Bull, Johns Hopkins
on motoneurons

P. 781G

Phil's comments.

Anatomy — relate high frequency occurence of these small things we regard as gemmules with the Golgi frequency of spines or gemmules.

+ low freq of recurred collat.

mitral to mitral can be excluded for ~~trunks~~ but could no be sure of terminals.

non-firing & firing should be clearly not alternate firing & non firing.

little more detail on the two inhibitions. Why wouldn't these current flows interfere or obscure each other

Footnote on computational simulation

Granule cell core conductor is answer to

photo, to show prevalence of granule dendrite ~~spines~~ in space between mitral cell bodies

implication for presynaptic inhibition & inhib go across p.183a

K.F. thinks recurrent really means recurrent collateral only

K.F. especially interested in passive aspect of this model.

With antidromic, remember that even when one initial blocks others could fire

But really, I am assuming large pop. activity. May need to bring this out more clearly.

Phil mentioned that n.m. jcn miniatures more frequent as endings are depol.

~~[illegible]~~

J. Physiol — approx 57 or 58

del Castillo & Katz

124, 586-604 1954b

Liley 134, p.427-443 1956

1859

Main point of hypothesis

(1) Dendro-dendritic granule & mitral sec.

(2) Dual polarity – E mitral → granule
J granule → mitral

(3) Thus granule ~~dendrites~~ serve ~~as~~ both receiving & sending role as ~~an~~ interneuron subserving lateral inhibition.

Synapses of Dual Dendro-Dendritic Polarity between Mitral and Granule cells of Olfactory Bulb.

~~Synaptic pathway~~

Synaptic inhibitory pathway mediated ~~involving~~ by dendro-dendritic synapses ~~of~~ both orientations

185b

It seems that
Yamamoto + Iwama (1962)
Green et al (1962)

attributed ~~initial~~ inhibition to a direct connection from ~~of~~ recurrent collaterals to mitral secondary dendrites.

while
Orrego (1961) – turtle bulb
Phillips, Powell & Shepherd (1963)
Shepherd (1963)
Yamamoto, Yamamoto & Iwama (1963)

postulate granule cell interneuron which is excited by collateral, but itself excites the mitral secondary dendrites.

3 msec min. latency

Our model is very similar, but provides a better explanation of points that ~~troubled~~ were found troublesome by these others esp.

(4) Green et al ruled out a Renshaw cell, but not the idea of sustained action granule cell.

(3) The periodic following & non following ~~of~~ the antidromic invasion, they thought would not fit interneuron, will fit our model OK.

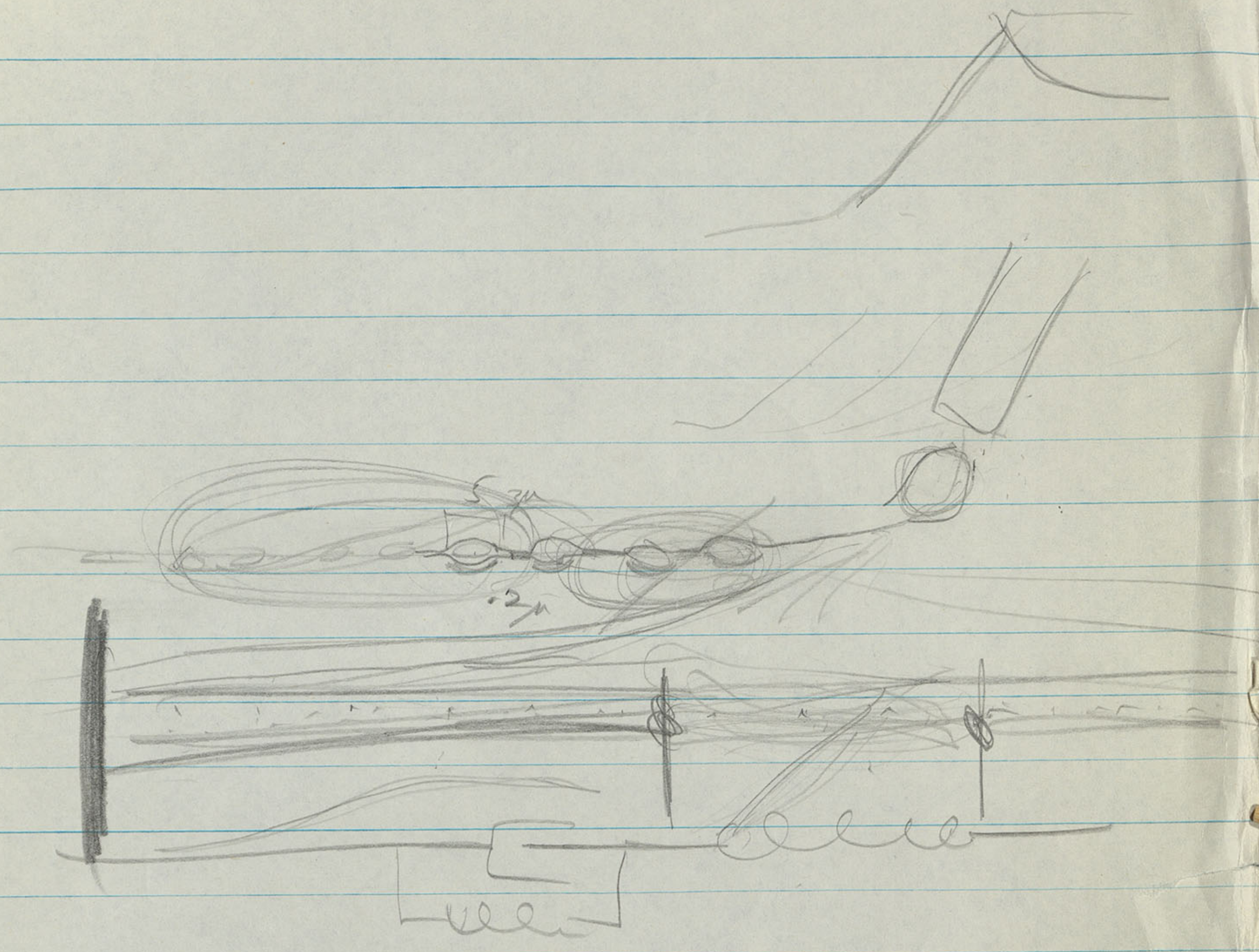
(1) Yamamoto AC stim builds up inhib much more than LOT
also LOT will not add to this ~~[illegible]~~ IPSP {Problem pattern, not us

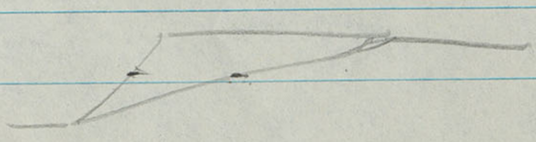
Phillips, Powell & Shepherd p. 85

argue that 3 to 50 msec latency suggests presence of at least one interneuronal step

p. 86 - inhib self limited

p. 105 following strong shocks


5 μ
.2 μ



Yamamoto, Yamamoto & Iwama

Also Orrego want granule cell to mediate inhibition.

But there is extra complication with AC – Anterior Commissure – stim,

which, however, Tom says will not stim Tufted cells, according to Valverde.

Vol 65 530-561 #4

German paper

Feb. 65 Zeitschrift for Zellforschung

~~Yamoto~~ Yamamoto

granule cells epsp

J. Neurophysiol 1963
Vol 26, p. 403

epsp in granule cells that come on with J.

~~J. Neurophysiol.~~
Vol 25, 1962

Green p. 467, — — Von Baumgarten

cut tract in advance to degenerate centrifugal fibers.

Second article later.

Clark Renshaw story duration

Ant. Commissure → Deep granule dendrites

axon plexus
stellate axons
~~Tufted~~ recurrent collaterals
initial collaterals
numerous centrifugal fibers

→ granule cell body

Archiv anat Histol. Japan Vol 24

Hirata

II fine atypical types

(a) vesicles both sides ext. plex. + mitral layer.

i.e. dendrodendritic

(b) mitral soma + granule.

in some cases soma presynaptic

(c) bipolar a single process is both pre + post synaptic. ext. plexiform

(d) serial synapse — or axo-axonic

? inhib. Gray type 2

(e) Subsynaptic Cisterni

Allison, A.C.

Morphology of olfactory system of vertebrates.

Biol. Rev. 1953

28: 195–244

Ask Mills

About travelling Gordon from Boston to here for two weeks

Also – 21 day excursion supplement ?

Then for next November 1965

for 6 months to 1 year temporary apptment

? Visiting Scientist

? Reactivate Commission

? Temporary Civil Service

did he ever submit his form 57

? Staff Fellow

Foy & O'Brien pp 888–890 in Feb 19, 1965 issue of Science

Duplication of Evoked Potential Waveform by the Curve of Probability of Firing of a Single Cell.

Micropipette in Cat cerebral cortex

Problem behind all this is the relation of evoked potential to pattern of single cell firing. Even more so explanation of evoked potential.

Problem has slight relation to Roll & Hunt paper.

There – pop. response was clearly sum of spikes.

This ~~study~~ covers evoked potential over ~~about~~ 2/3 of a second, ∴ assumed to be due to sequential activity of neurons, presumably in vicinity.

Their unit profile is really a histogram of spike no. vs t (5000 sweeps)

& this resembles averaged field potential after killing unit.

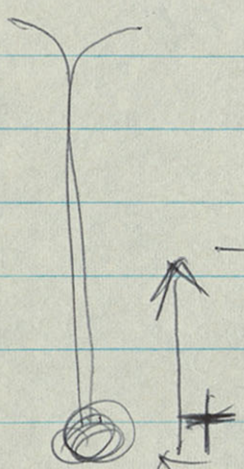
Did tapping cause destruction of cell? Suppose so.

Not sure what the polarity of their evoked potential record is, but could check Chokha Li's

Chang says primary resp. is surface (+) ∴ Foy & O'Brien seem to have surface vs focal ∴ neg. assoc. with heightened firing probability?

it seems that as little as 100 μV in evoked pot. can cause sign increase in probability of firing. factor of at least 5

What would I predict in connection with my thoughts about granule mitral interaction



If recording from near soma, relative to cortical surface, a pos. field pot. implies current flowing radially toward surface.

~~p59~~ suppose ψ const.

for Rheobase

$$\frac{\mathcal{E}}{V^2} = \frac{R_1+R_2V^2}{R_3+R_4 g} = \frac{1}{V(1-V)} + \frac{g(V+.1)}{V^2(1-V)} - \frac{\psi}{V^2(1-V)}$$

$V-V^2$

Note that $\psi > 0$ means current from inside to outside which is cathodal

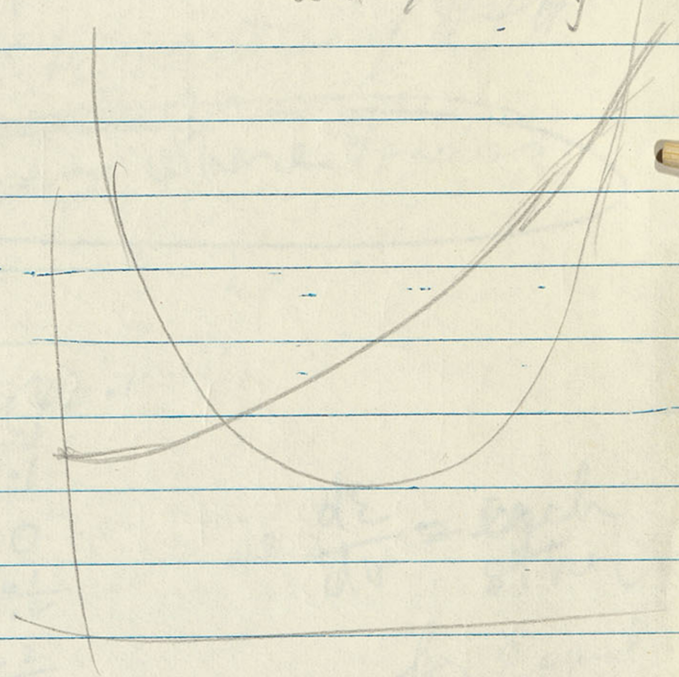
$\frac{I_m}{E_c - E_r}$

~~Eg~~ i.e. ψ pos is cathodal and excitatory

~~effect of neg~~ ψ^*

if $g = 0$

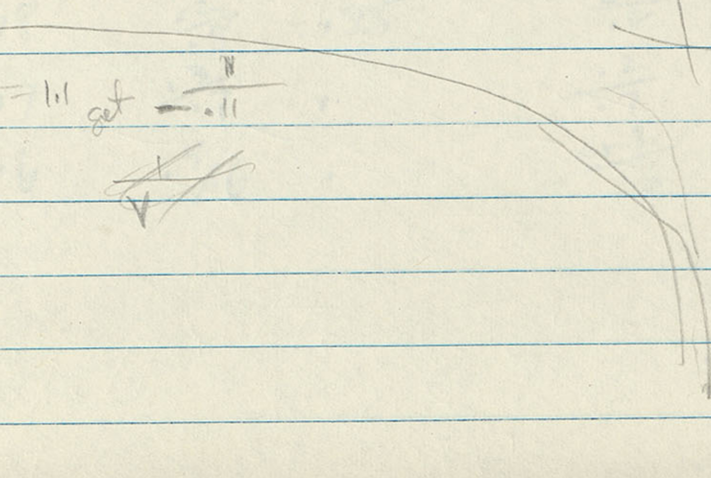
effect of ψ^* would be



~~if V = .1~~

and $(1-V) = 1.1$ get $-\frac{N}{.11}$

$\cancel{\frac{\psi}{V}}$

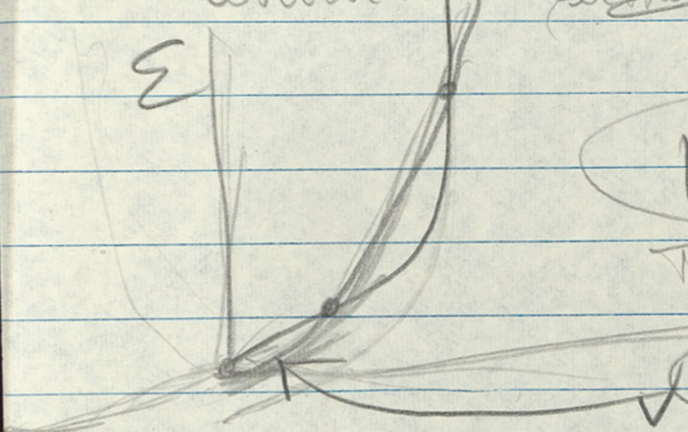


E must be smaller by $\frac{\Psi}{1-V}$

If $\dot{V}$ is to be zero when $\Psi > 0$

then $-V + (1-V)\,\mathcal{E}$ must be more neg

which means ~~either or both~~ ($\mathcal{E}$ smaller



p. 91 of Book 3

Topological properties of H&H

rheobase is where touches.

$\frac{V-\Psi}{1-V}$

.1

suppose $\Psi = .1$

V	$1-V$	$\frac{V}{1-V}$	0	$\frac{V-\Psi}{.1}$
.1	.9	$\frac{.1}{.9}$ =	.1111	0
.2	.8	$\frac{.2}{.8}$	.25	$\frac{.1}{.8}$
.3	.7	$\frac{.3}{.7}$	.	$\frac{.2}{.7}$
.4	.6	$.4/.6$	.	$\frac{.3}{.6}$

ie $\frac{d\mathcal{E}}{dV}$ = ~~each~~ other

for $\mathcal{E}$ equal each other

~~those~~ Those known to occur in normal ionic media.

~~One of the simplifying notions is to obtain the delay in~~

~~The computational simplicity is achieved by avoiding computation of exponential functions and~~

Exponential functions are not used in the computations; steep rises are obtained by autocatalytic growth, delay is obtained by making the growth of a quenching conductance depend upon the presence of excitatory conductance, ~~and rapid fall~~

The system of equations can be sketched outlined as follows:

$$\dot{v} = \qquad (1)$$

$$\dot{\varepsilon} = \cancel{P}F_1(v) - \cancel{Q}F_2(\varepsilon, g) \qquad (2)$$

$$\dot{g} = F_3(\varepsilon g) - F_4(g) \qquad (3)$$

where (cf. Rall, 1962, 1964)

$$v = (V_m - E_r)/(E_\epsilon - E_r) \qquad (4)$$

we wish to provide

we wish this

is displaced beyond its threshold value (say 0.2), we must arrange that this will cause the value of $\mathcal{E}$ to grow.

The growth of the action potential ~~must~~ involves ~~([illegible])~~ ~~first~~ a growth in the value of $\mathcal{E}$, ~~which~~ ~~is~~ and this causes the term $(1-v)\mathcal{E}$ in equation (2) to contribute a growth rate which exceeds the passive decay term. Suppose $v = 0.3$; then the passive decay rate is -0.3 while the growth term is $0.7\,\mathcal{E}$. As both v and $\mathcal{E}$ grow and approach their peak values, for uniform patch of membrane ~~[illegible]~~

Specific System can be written

$$\frac{dV}{dT} = \mathcal{E}(1-V) - j(\beta+V) - V + \cancel{I}$$

$$\frac{d\mathcal{E}}{dT} = k_1 V^2 + k_2 V^4 - (k_3 + k_4 j)\mathcal{E}$$

$$\frac{dj}{dT} = k_5 (k_3 + k_4 j)\mathcal{E} - k_6 j$$

$T = t/\tau$

$V = (V_m - E_r)/(E_\epsilon - E_r)$

$\mathcal{E} = G_\epsilon/G_r$

$j = G_j/G_r$

$\beta = (E_j - E_r)/(E_\epsilon - E_r)$

3/26/64 5/21/64

Book 4 p. 8, p. 35

Book 3 p. 4 p. 11 p. 21 p. 26

9/26/63 10/22/63 11/11/63 11/29/63

p. 51 neg. values troubles p. 63

1/10/64

Table of Symbols

Dimensionless Quantities:

3 $v = (V_m - E_r)/(E_\epsilon - E_r)$ = normalized deviation of membrane potential from its resting value

1 $\mathcal{E} = G_\epsilon / G_r$ = measure of excitation

2 $\mathcal{J} = G_j / G_j$ = measure of quenching or inhibition

5 $\chi = I_m R_m/(E_\epsilon - E_r)$ = measure of net membrane current

4 $\beta = (E_j - E_r)/(E_\epsilon - E_r)$ = ~~value of v~~ ~~[illegible]~~

= constant = value of v when $V_m = E_j$.

6 $T = t/\tau$ = time expressed relative to passive membrane time constant.

Predictions for Ted Lewis

I 1957 note to *Science* predicted $\tau \longrightarrow 4$ msec

delayed current $\longrightarrow \epsilon$

1960 presented theory for linear plot $\log\left\{V_T \frac{dV}{dt}\right\}$ vs t

over range from $t = \tau$ to $t = 2\tau$

These predictions have been confirmed both in my 1960 paper, and even by Eccles 1961 paper

II In the 1955 theoretical paper in J. Cell. Comp. Physiol, figs 1 and 2 illustrate predictions, while Fig. 4 presents an approximate experimental verification. Figs. 5, 6 and 7 were also verified in a general manner, but have not been followed up further. The crux, at the time, was discussed on pp 401-404, plus the fact that only a single parameter had to be adjusted to fit the family of curves,

III In 1956 (Rall and Hunt, J. Gen. Physiol. 39, 397-422) we presented a theoretical model on pages 414-420 designed to fit Figs 1-8 and the first four columns of Table I. The theory predicted what was verified by Fig. 9, and in fact, the prediction was made before the figure.

IV In the 1960 paper, IPSP ~~time course~~ was shown to be consistent with the possibility of generation near the soma.

Also, 1962 NY. Acad. paper points to greater effectiveness of inhibition near soma.

More recently, Eccles claims to have evidence for this ~~from~~ several systems.

V The predicted dependence upon distance of peak extracellular negative potential 1962 - Biophys J. Fig. 10, curve F was approximately verified by comparisons with data of Nelson and Frank. Also The time course (Fig. 11), esp. the positive component were predicted for passive dendrites, in approx. agreement with Frank & Nelson: see their paper in J. Neurophysiol 27, 913-927 (1964)

Some of the details which were presented at the Intl. Biophysics Congress in 1962 have not yet been published.

(Abstract for First Lecture)

Theoretical Significance of Dendritic Trees for Neuronal Input-Output Relations. (Wilfrid Rall, National Institutes of Health, Bethesda, Md.)

Neural modelers have generally assumed that the synaptic input to a neuron can be treated as input delivered to a single point; thus they have neglected the extensively branched neuronal receptive surface. There has also been a tendency to assume that a combination of synaptic excitation and inhibition can be treated as a simple arithmetic sum of positive and negative input components; this neglects known properties of nerve membranes. It is the purpose of this talk to draw attention to theoretical models which avoid these oversimplifications, and to present the results of computations designed to test the significance of what may be called spatio-temporal patterns of synaptic input.

(Abstract for Second Lecture)

Some Problems in Developing a Theory of Dendritic Neurons.

(Wilfrid Rall, National Institutes of Health, Bethesda, Md.)

The development of a mathematical model of dendritic neurons represents an attempt to combine three different kinds of knowledge into a coherent theory: (1) the anatomical fact of extensive dendritic branching, (2) theoretical models of nerve membrane, and (3) quantitative electrophysiological information that has been obtained from individual neurons by means of intracellular and extracellular microelectrodes. Consideration will be given to such problems as (a) choice of simplifying assumptions, (b) fundamental parameters related to time, to dendritic length, and to dendritic diameters, (c) consequences for physical intuition, (d) future for computation and testing.

Might a short paper to Theoretical Biology

for Gordon Conference

CNS systems composed of ~~neurons~~ assemblages ~~of~~

not of relays or adders

The neurons themselves have logical properties.

Assemblage of dots — connected.

Then say, oh well, can let several dots represent a neuron. This does not work without considerable mod. because effect of one neuron on other ~~tends~~ to be all or nothing per impulse ~~[illegible]~~ and unidirectional, while ~~the effect of~~ neighboring compartments of same neuron affect each other continuously & bidirectionally. Perhaps should pursue formulating this mathematically

? i.e. could have matrix with different ~~[illegible]~~ of elements. i.e. for electrotonus $\mu_{ij} = \mu_{ji}$

for impulses $\mu_{ij} = \delta_{ij}$ ~~while~~ $\mu_{ji} = 0$

Potency of Synaptic Inhibition

Factors in the Potency of Synaptic Inhibition

It is recently become fashionable to

The notion that synaptic inhibition should be more effective when delivered ~~to the neuron soma~~ to the soma than to the dendritic periphery of a neuron is now several years old, and has recently become very fashionable.

Check Lorente & Tasaki on cortical layers

Check Mueller on kinetics